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Tumors of the Testes

Five-year Follow-up Study

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ALTHOUGH malignant tumors of the testicle are relatively rare, these neoplasms pose a particularly serious problem to military medicine. They occur in the third and fourth decades of life during the period of maximum productivity; the incidence is at its peak in the late twenties. Among Army personnel the incidence was found to be about 1 in 10,000; we found a similar incidence among Navy personnel.

HISTOGENESIS

Because the variety of histologic types of testicular tumors indicates that germinal tissue or gonocytic cells provide the origin for these new growths, one can theorize that the developmental potentialities of this tissue corresponds to the pathway of differentiation followed by the fertilized sex cell. The tissue of origin is totipotential and is capable of developing along lines similar to those found in the earliest phases of differentiation in the fertilized ovum or zygote. As shown in figure 1, the fertilized ovum pursues three separate lines of development. The earliest to be completed is trophoblastic differentiation which

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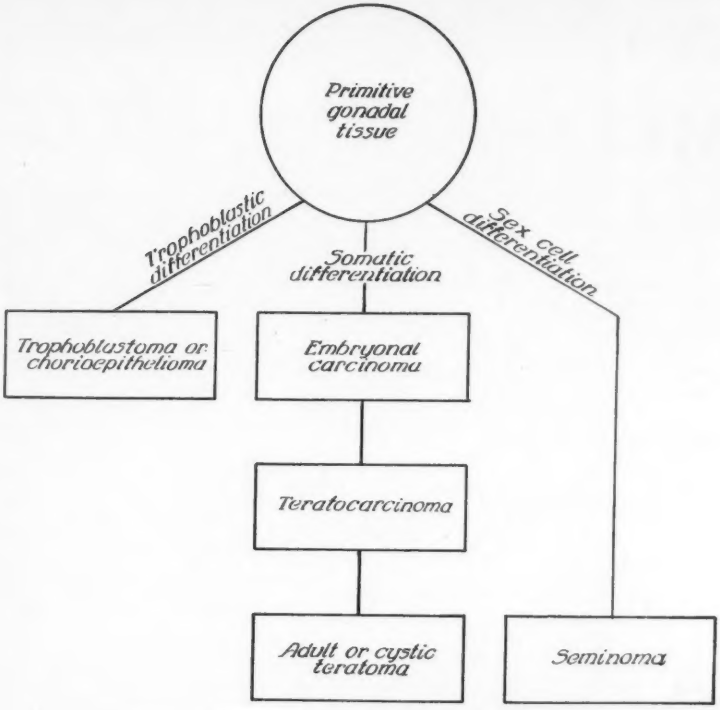

Figure 1.—Theory of histogenesis of testicular tumors.

forms placental tissue. Trophoblastic differentiation is represented among testicular tumors by chorioepithelioma or trophoblastomas. The second line of differentiation is concerned with embryogenesis and consists of the elaboration of the three germ layers. This is represented among testicular tumors by embryonal carcinoma, teratocarcinoma, and adult teratomas. The third line of development is concerned with the formation of reproductive tissue for subsequent generations and for the perpetuation of gonocytic tissue and is represented among testicular tumors by the seminomas.

HISTOPATHOLOGY

Following the lead of Ewing (*1*) in 1911 the trend in pathology was to disregard the histologic subclassification of malignant neoplasms of the testicle and to group them as malignant embryomas or teratomas, chiefly because an admixture of cell types could be demonstrated in a given case. In 1931, however, Ferguson et al. (*2*), studying the hormonal output of the urine in patients with testicular tumor, reemphasized the desirability of subdividing these malignant growths.

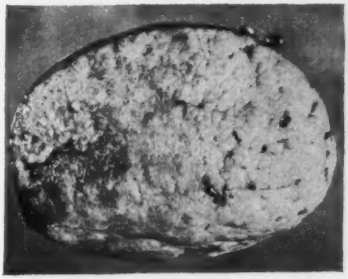

Figure 2.—Gross specimen of testicular seminoma. The cut surface of the tumor is granular and resembles somewhat the normal testis.

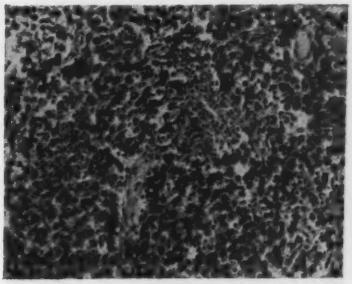

Figure 3.—Low-power photomicrograph of seminoma. The cellular components stand out individually and are embedded in lymphoid stroma. × 100.

There is now a general agreement that the behavior and prognosis differ for teratomas, seminomas, and embryonal carcinomas—the most common types of testicular malignancy.

Seminoma is usually a slow-growing testicular mass. The history of swelling of the testicle may date back as long as 5 years; the average is 14.5 months. Grossly it is a granular, fleshy, yellow mass resembling the neighboring testicular tissue (fig. 2). Microscopically it is composed of rather uniform rounded to polyhedral cells occurring in large sheets. The cells have a distinct border, a centrally placed vesicular nucleus, and usually a distinct nucleolus. The cytoplasm is clear, taking a faintly eosinophilic stain with hematoxylin and eosin. In many instances a lymphocytic infiltrate is scattered throughout the tumor areas (figs. 3, 4, and 5).

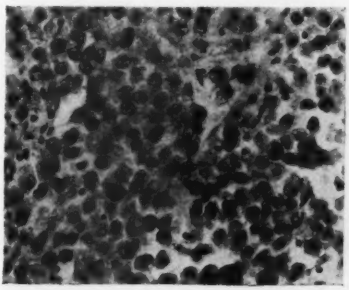

Figure 4.—Medium-power photomicrograph of seminoma. The nuclei and cytoplasm are of moderate size with an occasional large nucleus. × 200.

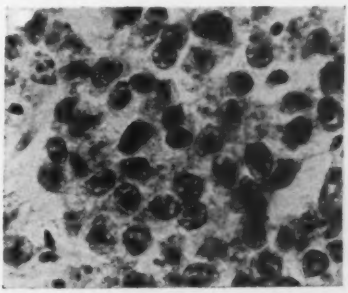

Figure 5.—High-power photomicrograph of seminoma. The nuclear pattern resembles that seen in embryonal carcinoma (fig. 12). The cytoplasm is granular and has indefinite borders. There is no attempt at alveolar formation. × 400.

Adult teratoma and teratocarcinoma are solid or cystic testicular tumors which at times may seem to contain fluid on palpation depending upon the size of the cystic areas (fig. 6). In our cases, the history of a swelling of the testicle dated back 4.5 to 5 months. The adult type neoplasm grossly is well-circumscribed with a definite capsule separating the neoplasms from the surrounding testicular tissue. Microscopically, they are made up of a variety of structures with adult epithelium, cartilage, and smooth muscle predominating (figs. 7 and

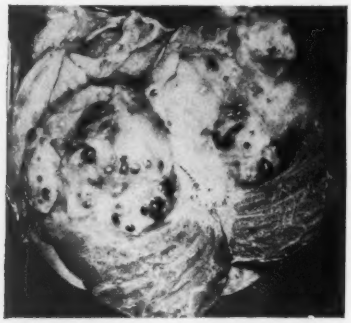

Figure 6.—Gross specimen of cystic teratoma of testis. The cystic components of the tumor bulge from its cut surface. The white fibrous structure of the neoplasm is clearly demarcated.

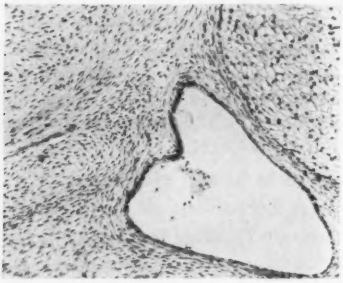

Figure 7.—Adult testicular teratoma showing the dense fibrous stroma and a cyst lined by low columnar epithelium. × 50.

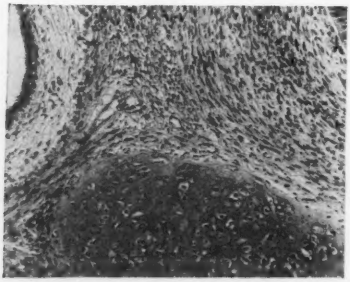

Figure 8.—Adult testicular teratoma showing the characteristic primitive fibromuscular stroma, islands of hyaline cartilage, and cysts lined with ciliated epithelium. × 100.

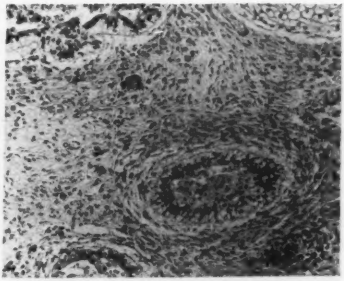

Figure 9.—Testicular teratocarcinoma. This pleomorphic tumor contains islands of squamous epithelium and mucinous glands embedded in cellular fibrous stroma. × 100.

8). Occasionally neurogenic tissue, osseous and various glandular components may be encountered. In general, the adult teratomas present histologic features in one or more areas that resemble those found in teratocarcinoma. The teratocarcinoma grossly resembles the

adult type but, in addition, areas of necrosis and hemorrhage are usually seen. Microscopically, all the elements present in the adult teratoma may be present but the individual elements, particularly the epithelium, take on malignant characteristics (figs. 9 and 10). Areas of chorionic tissue and embryonal carcinoma may be a conspicuous feature. In the final analysis the subclassification of teratomas into adult and carcinomatous forms is of doubtful value. In our opinion both groups are malignant, the degree of malignancy varying with the amount of chorionic and embryonic tissue present. The embryonic tissue usually takes the form of embryonal carcinoma or neuroepithelioma.

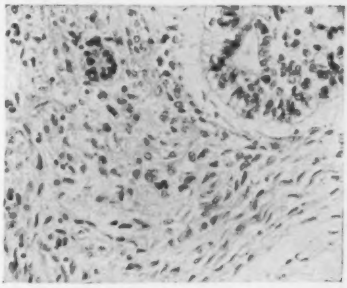

Figure 10.—Medium-power photomicrograph of the teratocarcinoma shown in figure 9. × 200.

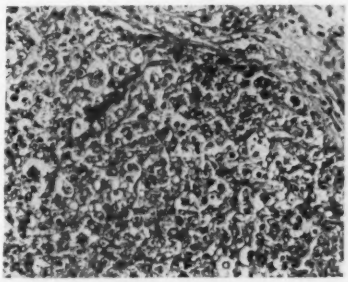

Figure 11.—Testicular embryonal carcinoma. The tumor is forming alveolar spaces surrounded by cells of varying shapes and sizes, containing irregular hyperchromatic nuclei. × 100.

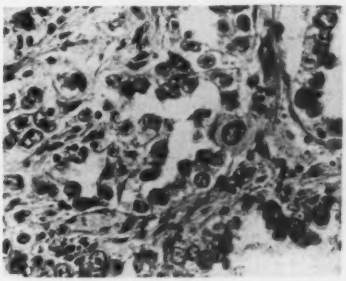

Figure 12.—High-power photomicrograph of embryonal carcinoma shown in figure 11. The alveolar pattern is clearly shown. × 400.

Embryonal carcinoma forms a solid, rapidly growing mass which may be complicated by hemorrhage and tenderness. In our cases the duration of symptoms prior to examination was approximately 7 months. Grossly this carcinoma is a soft, necrotic, or hemorrhagic tumor mass ill-defined from the surrounding tissue. Microscopically it is composed of large epithelial cells occurring in a variety of cellular and acinar patterns. Occasionally the cells may be of uniform size and appearance, but more frequently there is considerable pleomorphism. The cells are larger than the cell making up the seminoma and vary in appearance from cuboidal to polyhedral. The nuclei are large and hyperchromatic (figs. 11 and 12). In this type,

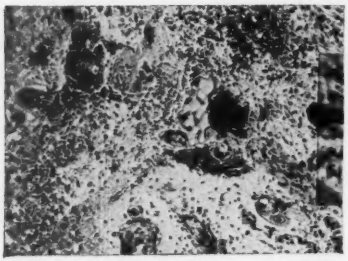

Figure 13.—Testicular chorioepithelioma or trophoblastoma. Characteristic islands of syncytial cells adjacent to vascular spaces. Sheets of cytotrophoblasts are also present. × *100.*

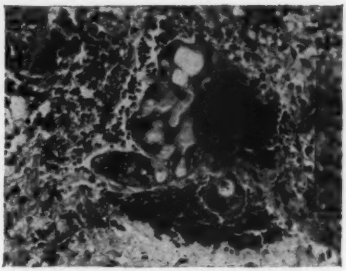

Figure 14.—Testicular chorioepithelioma. Same as figure 13. × *300.*

large bizarre cells representing the remnants of trophoblastic tissue are frequently encountered.

Chorioepithelioma of the testicle in pure form is rare, and signs of metastases associated with a positive Aschheim-Zondek test may precede the discovery of the primary mass. The surgical specimen shows soft, hemorrhagic, ill-defined neoplastic masses occupying a small portion of the testis. Microscopically the picture is characteristic (figs. 13 and 14). Two cell types are usually present, the large irregular hyperchromatic syncytiotrophoblast and the more regular, oval or cuboidal cytotrophoblast. In most areas there is no cell pattern but in some instances there are attempts at formation of typical chorionic villi. Hemorrhage is a prominent microscopic feature.

The mortality rate from these neoplasms has always been considered to be extremely high, however, no adequate studies of a large series of cases have been reported prior to the last war. In 1946 Friedman and Moore (*3*) reported 922 cases of testicular tumors observed for a period up to 1 year. During that period the mortality rates for this group were 27.5 percent for embryonal carcinoma, 17 percent for teratocarcinoma, 15 percent for teratoma, and 2.5 percent for seminoma. In 1947 Gordon-Taylor and Wyndham (*4*) reported 636 cases of testicular tumors; 38 percent of the patients were dead within 1 year and 55.5 percent within 5 years. The death rate in individual types of testicular tumors was not given, nor were the details of the follow-up data on which their conclusions were based. Lloyd Lewis (*5*) in 1948 reported that 24 percent of 169 patients with all types of testicular tumors treated between May 1942 and July 1946 by radical orchiectomy were dead at the end of approximately a year and a half.

Recently Sauer and Burke (*6*) reported that the over-all cure rate in their series, based upon a review of 202 cases of testicular tumor admitted over a 25-year period (1 January 1922 to 31 December 1946)

was 47.5 percent. The 5-year cure rate was 48.9 percent in 143 patients admitted prior to 31 December 1941. The cure rates for the various types were as follows: adult teratoma, 80.0 percent; seminoma, 59.6 percent; teratocarcinoma, 44.4 percent; and embryonal carcinoma, 22.5 percent.

CLASSIFICATION

This study is based upon 229 cases of testicular tumors, 216 of which fall into the classification of either seminoma, teratoma, or embryonal carcinoma. Of the 216 cases; 162 had been observed a minimum of 5 years or until death (table 1); 12 cases of miscellaneous tumors had been observed a comparable length of time. Only those cases in which microscopic study permitted classification of pathologic type and in which there was adequate follow-up data have been included. We found that the percentage distribution for the various types is comparable to that of Friedman and Moore (*3*) who studied a much larger group and that seminoma, teratoma, and embryonal carcinoma occurred with about equal frequency among 229 cases (fig. 15).

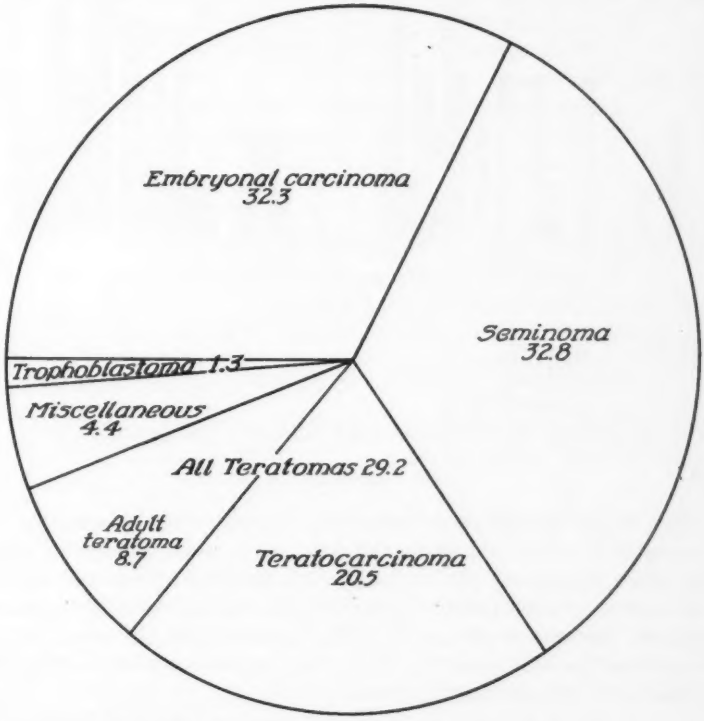

Figure 15.—Percentage distribution of testicular tumors.

TABLE 1.—*Follow-up in 216 cases of tumor of testes*

Total number of tumors	Time followed in each case	Seminoma			Teratoma			Embryonal carcinoma		
		Number followed	Total number dead	Mortality	Number followed	Total number dead	Mortality	Number followed	Total number dead	Mortality
				Percent			*Percent*			*Percent*
216	6 months	75	6	8.0	67	4	5.9	74	23	31.1
214	1 year	74	11	14.9	67	18	26.9	73	36	49.3
213	2 years	73	19	26.0	67	29	43.3	73	51	69.9
205	3 years	69	21	30.4	63	31	49.2	71	55	77.5
182	4 years	61	21	34.4	55	34	61.8	67	56	83.6
162	5 years	52	21	40.4	45	34	75.6	65	56	86.2
149	6 years	46	22	47.8	42	35	83.3	61	56	91.8

The testicular tumors forming the basis of this study were classified histologically as follows:

Gonocytic series:

1. Seminoma:
   - *a.* Typical.
   - *b.* With lymphoid tissue.
2. Adult teratoma:
   - *a.* Typical cystic.
   - *b.* With mesenchymal tissue predominating.
3. Teratocarcinoma:
   - *a.* Teratoma with neuroblastic tissue predominating.
   - *b.* Teratoma with embryonal carcinoma predominating.
   - *c.* Teratoma with chorioepithelioma.
4. Embryonal carcinoma:
   - *a.* Typical or pure type.
   - *b.* Embryonal carcinoma with seminoma.
   - *c.* Embryonal carcinoma with chorionic tissue.
5. Chorioepithelioma or trophoblastoma.

Nongonocytic series:

1. Androblastoma (derived from Sertoli cells).
2. Interstitial cell tumor.
3. Lymphangioma or adenomatoid tumors of epididymis.

AGE DISTRIBUTION

The origin of testicular tumors is related to the maturation of testicular function. Gonadal development is at its maximum from the onset of puberty at about 13 or 14 years of age to the end of adolescence at about 16 or 17 years of age. Sexual maturity appears between the ages of 18 and 25. The highest incidence of testicular tumors occurs after sexual maturity during early adulthood, ages 26 to 35, rather than during adolescence.

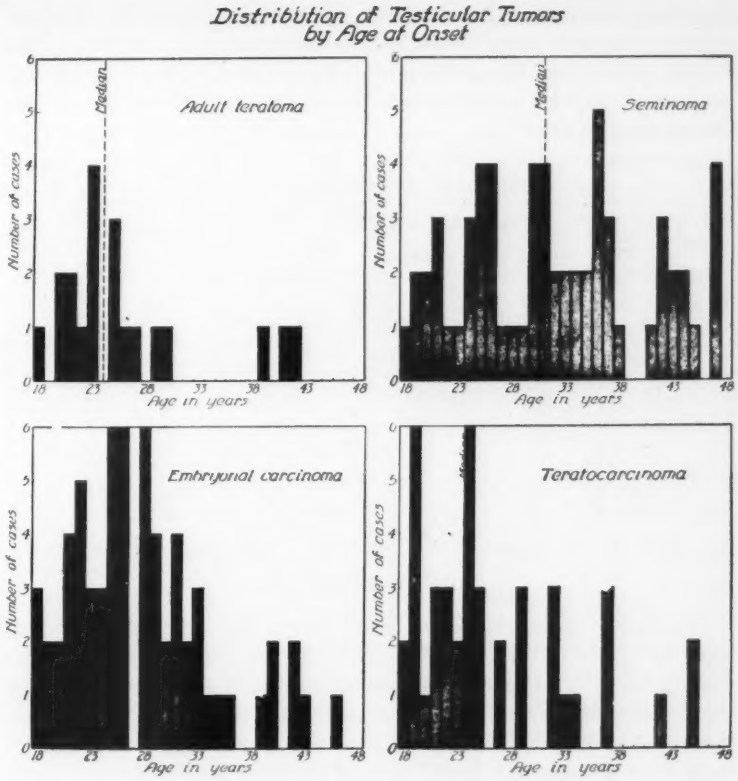

Figure 16.—Median age groups.

In our series a study of the age distribution for the four types (table 2) showed that seminoma occurred comparatively much later than the other three types (fig. 16).

The age distribution shows the median to occur as follows: (*a*) seminoma, 31 years; (*b*) teratoma and teratocarcinoma, 24 years each; and (*c*) embryonal carcinoma, 26 years.

There is a difference of 7 years between the median age of seminoma and of the teratomas. This closely approximates the findings of Friedman and Moore who found a 5-year difference between the mean age for seminoma and teratocarcinoma. Embryonal carcinoma occurred somewhat later—about 2 years—than the teratomas. In our series the incidences were not corrected for the population distributions of the various age groups. In addition to Navy personnel some of the

cases were Veterans' Administration patients and some were civilians and the total population represented by these cases is not known. The median rather than the arithmetic mean was used owing to a limited number of extreme values which would distort the true nature of the age distribution.

TABLE 2.—*Age distribution in 189 cases*

Age	Seminoma	Adult teratoma	Teratocarcinoma	Embryonal carcinoma	Age	Seminoma	Adult teratoma	Teratocarcinoma	Embryonal carcinoma
18	1	1	2	3	35	2	0	0	1
19	2	0	6	2	36	5	0	0	1
20	2	1	2	2	37	3	0	3	0
21	3	2	3	4	38	1	0	0	0
22	1	1	3	5	39	0	1	0	1
23	1	4	2	3	40	0	0	0	2
24	3	0	6	3	41	1	1	0	0
25	4	3	3	6	42	3	1	1	2
26	4	1	0	6	43	2	0	0	1
27	1	1	2	0	44	2	0	0	0
28	1	0	0	6	45	1	0	2	0
29	1	1	3	4	46	0	0	0	1
30	4	1	0	2	47	4	0	0	0
31	4	0	0	4	48	0	0	0	0
32	2	0	3	2					
33	2	0	1	1	Total	62	19	43	65
34	2	0	1	1					

CLINICAL FEATURES

The clinical symptoms of testicular tumors are indefinite. A painless swelling of the testicle which enlarges gradually over months or years is the rule. The tumor affects the body of the testicle rather than the epididymis. Pain is associated only with trauma or hemorrhage. Symptoms of longer duration occur in the more slowly growing tumors, such as the seminomas. In 169 cases of our series the duration of symptoms prior to operation was given. In cases of seminoma it was 14.4 months; in embryonal carcinoma it was 6.9 months; and in teratoma and teratocarcinoma, it was 4.8 and 4.6 months respectively.

Cryptorchism was not an important feature in our series. Patients with undescended testicle are not accepted for naval service. However, cryptorchism was present in three cases of seminoma; but these were cases in civilian persons included in our study.

Bio-assay for gonadotropic hormones was helpful for diagnosis in only an occasional case, which was either a frank chorioepithelioma or where chorionic tissue was contained in tumors having the pathologic features of teratocarcinoma or embryonal carcinoma.

TREATMENT

The treatment in these cases has been standardized in the past 20 years in naval hospitals, and consists of ligation of the cord at the

internal inguinal ring and excision of its distal portion along with the testicle. This is followed by external irradiation therapy through multiple ports by the divided dose technic, using 250 kv. A total of between 8 and 10 thousand roentgen units is given to the node-bearing areas—the right and left inguinal regions, and the hypogastric and preaortic group up to and including the region at the bifurcation of the aorta. The details of the operation were available in every case and in no case was radical orchiectomy performed (removal of the

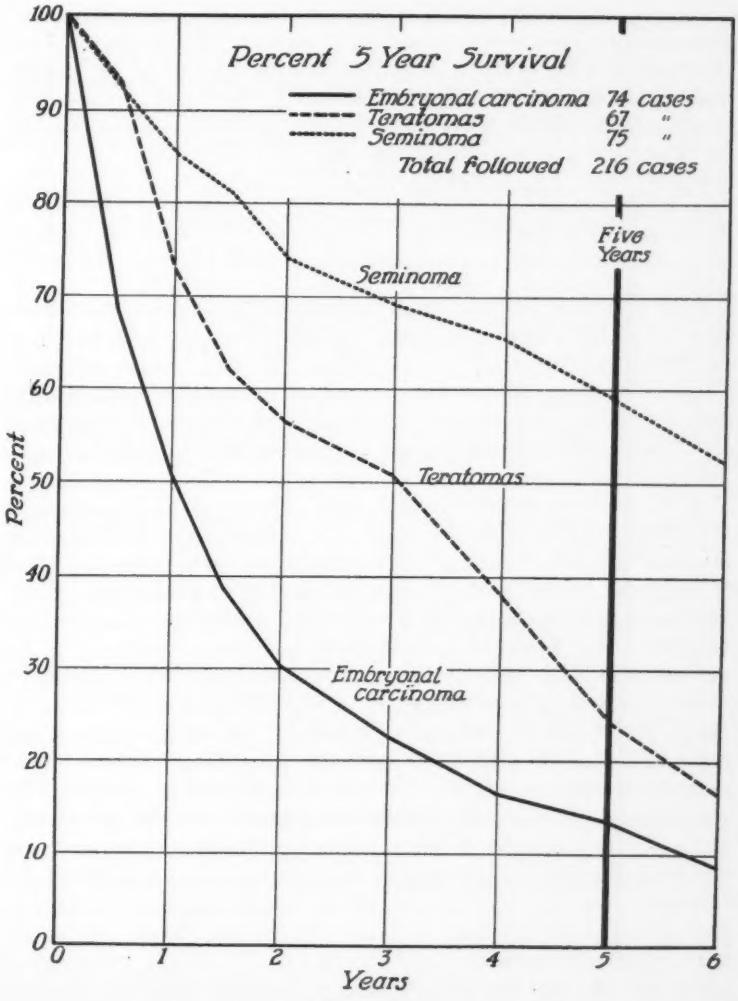

Figure 17.

testes, the entire spermatic cord, and the retroperitoneal lymph chain from the inguinal ring to the renal pedicle). However, in two cases bilateral orchiectomies had been performed. Less adequate data were available on the technic of irradiation. However, in 80 percent of the records postoperative irradiation was in accordance with that previously noted.

END RESULTS

The 5-year survivals in seminoma are approximately 60 percent; in teratomas, 24 percent; and in embryonal carcinoma, only 14 percent. The over-all 5-year survival rate is 31.7 percent. The mortality rates are greatest in the first and second years after operation. Of the 216 cases, 148 have been followed a minimum of 6 years; they are presented graphically to show that the general mortality trend continues beyond the "five-year" survival period (fig. 17).

The number of cases of pure chorioepitheliomas, 3, and nongonocytic tumors, 10, is too small for critical statistical analysis.

DISCUSSION

Prior to recent years it was the consensus that seminomas constituted about two-thirds of all testicular tumors and that about 45 to 50 percent of patients with this condition survived 5 years or longer. The teratomatous tumors were considered to make up one-third of the total of the testicular new growths, and had a 5-year survival rate of about one-half that of seminoma. The reason for this misinformation was the inclusion of the embryonal carcinomas in the seminoma group. This distinction is sometimes made with difficulty and is an important one from the standpoint of prognosis. Friedman and Moore emphasized the importance of distinguishing between these two types of testicular tumors and our survival rates re-emphasize this point. Seminoma has a 5-year survival rate of 60 percent which is more than four times the 14 percent for embryonal carcinoma. Not only do the patients survive 5 years or longer but "permanent" cures are by no means rare and we have patients who had seminoma surviving 11, 12, 15, 17, 18, 20, and 21 years. An interesting case report in this group is the following: In 1929, at the age of 21, the patient had a unilateral orchiectomy for seminoma. In 1935 a seminoma appeared in the remaining testis for which a simple orchiectomy was also performed. He is living and well 20 years following the first surgery. Some writers believe that in contrast to seminoma, cures among embryonal carcinoma are exceedingly rare unless radical surgery is performed. Our statistics do not bear this out. There are records of patients with embryonal carcinoma who survived 6, 7, 8, and 11 years and of 5 patients who survived over 5 years; in these the treatment consisted

of unilateral orchiectomy and postoperative roentgen irradiation with 250 kv. In cystic teratoma and teratocarcinoma the survival rates lie between those of seminoma and embryonal carcinoma. Cures were recorded for both types of teratoma, and two patients with teratocarcinoma surviving 12 and 26 years and several with cystic teratomas living 10 to 11 years. Patients with trophoblastoma or chorioepithelioma rarely survive 5 years. There is one exception—a patient 23 years of age at time of operation who is living and well 6 years after treatment.

SUMMARY

The significant pathological features of tumors of the testes are as follows: (*a*) Seminoma has a uniform type of cell without particular arrangement in lymphoid stroma. (*b*) Teratoma shows islands of cartilage, and epithelial proliferation of either benign or of malignant character and may also show cyst formation. When malignant neuroepithelium, chorionic tissue, or cells resembling embryonal carcinoma are present the tumor can be classified as teratocarcinoma. When cysts lined by mature epithelium are present it falls into the classification of adult or cystic teratoma. From a practical standpoint it is probably not necessary to differentiate between these two. Both types are malignant although cystic teratoma has a slightly better prognosis. However, in our experience, if multiple sections are taken, most cases of cystic or adult teratoma will be reclassified as teratocarcinoma. (*c*) Embryonal carcinoma can be classified on the basis of large neoplastic epithelial cells in crescent or pseudo-acinar arrangement.

A tabulated summary of the features of testicular tumors is presented in table 3.

TABLE 3

Pathologic type	Total number of cases	Percent of all types	Median age	Average duration of symptoms	5-year survivals
			Years	*Months*	*Percent*
Seminoma	75	32.8	31	4.4	59.6
Teratoma	67	29.2	24	4.7	24.4
Embryonal carcinoma	74	32.3	26	6.9	13.8

Seminoma, teratoma, and embryonal carcinoma occur with about equal frequency in any large series.

The prognosis in both adult and carcinomatous varieties of teratoma is about the same.

Rare types of testicular tumors compose slightly over 5 percent of the total.

The 5-year survival rate of seminoma is 59.6 percent, and is twice the survival rate of 24.4 percent for teratomas and approximately four times the survival rate of 13.8 percent for embryonal carcinoma.

The over-all 5-year survival rate in testicular tumors is 31.7 percent.

Comparison of the results in this series with those in the literature show that unilateral orchiectomy followed by postoperative irradiation with 250 kv. is the treatment of choice; the survival rates are not enhanced by more radical surgery or more intensive irradiation.

There is a direct correlation between duration of symptoms and the degree of malignancy; especially in the case of the seminoma as compared with the other types.

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Torsion of the Spermatic Cord

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TORSION of the spermatic cord, commonly but incorrectly considered as torsion of the testis, is not rare. The recent admission to this hospital of three undiagnosed, and consequently neglected, cases has emphasized the necessity of increased awareness of this condition by all medical officers. Early diagnosis is important. The dispensary surgeon must be especially cognizant of the condition since he is in a position to diagnose this abnormality which is easily corrected if treated early. A delay of only a few hours in proper treatment means the difference between a necrotic, atrophic testis and the retention of a viable, functioning organ. Two of these cases are presented as illustrations of erroneous diagnoses. The third, with the same pathologic findings, treated conservatively elsewhere for 5 weeks is not described in detail.

CASE REPORTS

Case 1.—A 28-year-old man was admitted 20 days following an acute onset of pain in his left testis which occurred when he crossed his legs. He had received sulfadiazine and penicillin with slow regression in the extreme swelling of the left scrotal contents. On admission, the testis was about five times the normal size, was hard, and was suggestive of a tumor. Neglected torsion was

Figure 1.—Case 1. Torsion of left spermatic cord. A. Testis. B. Site of torsion. C. Tunica vaginalis and cord.

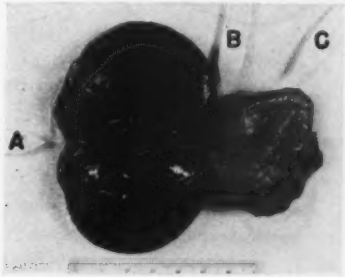

Figure 2.—Hemorrhagic infarction of testis. A. Testis. B. Site of torsion. C. Tunica vaginalis and cord.

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considered because of a history of at least three similar episodes of acute testicular pain, each of which terminated spontaneously after a short time. Surgical exploration demonstrated a 180° clockwise twist in the spermatic cord with infarction of the testis which required orchiectomy (figs. 1 and 2). The underlying bell-clapperlike deformity on the opposite side was corrected.

Case 2.—An 18-year-old man was admitted to this hospital 4 days after waking suddenly with a severe pain in his left testis. There was immediate swelling which subsided only slightly under treatment with bed rest, penicillin, and sulfonamides. Examination revealed an enlarged, firm testis and scrotal edema. Thickening of the spermatic cord immediately above the scrotum was minimal. Prostatic secretions showed 15 to 20 leukocytes per cubic millimeter. Surgical exploration demonstrated a torsion of the spermatic cord with infarction of the testis which required removal. The opposite testicle was treated as in the preceding case.

INCIDENCE

Undoubtedly the actual occurrence of this condition far exceeds the reported incidence. Ewert and Hoffman (*1*) collected 489 cases since the first formal report of this entity in 1840; they quote Wolf as having diagnosed the condition in a 68-year-old man. In the past 2 years the authors have observed three cases in infants ranging from 2 weeks to 16 months of age. Either side may be affected; in 24 of 350 cases collected by Ormond (*2*) torsion of the spermatic cord had occurred on both sides.

PATHOLOGY

Torsion of the spermatic cord never occurs in the normal testis, for in the normal scrotum it is impossible to rotate the testis to any great degree. In the usual type of torsion of the spermatic cord an abnormality, either developmental or acquired, exists. There are two

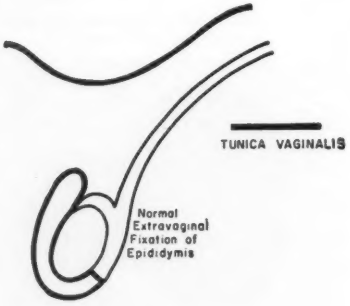

Figure 3.—Normal tunicary investment of the testis (after Muschat (3)). The tunica vaginalis covers the testicle and anterior part of the epididymis.

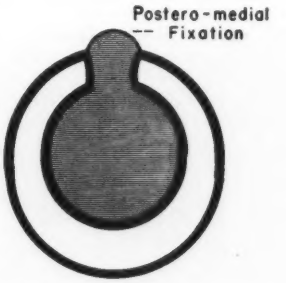

Figure 4.—Cross section of normal tunicary investment (after Muschat (3)). Note the extravaginal epididymis.

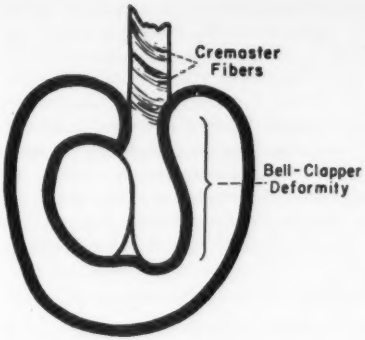

Figure 5.—Abnormality of tunicary investment in torsion (after Muschat (3)). The low extension of the cremaster in high investment of the cord which results in torsion is illustrated.

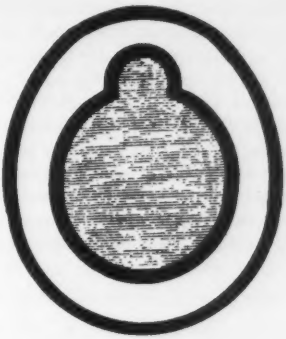

Figure 6.—Cross section of abnormal tunicary investment in torsion (after Muschat (3)). The testis and epididymis are freely movable in the vaginal sac, making rotation possible.

types: (*a*) extravaginal (rare) often associated with trauma, and usually associated with incarcerated hernia or as a result of direct trauma in cryptorchism; and (*b*) intravaginal (more common) amenable to surgical corrections when diagnosed early, and almost always associated with a scrotal developmental anomaly. Figures 3 and 4 demonstrate the normal tunicary investments of the testis. The posteromedial aspect of the epididymis normally lies outside the tunica vaginalis. Figures 5 and 6 show the commonly encountered abnormality that results in a free-lying testis and epididymis within the parietal tunica vaginalis.

The names "dangling testis," "floating testis," "intratunicary pedicle," and "bell-clapper deformity" have been applied to this deformity. An additional feature demonstrated by Muschat (*3*) is high investment of the cord by the tunica vaginalis with downward extension of the cremaster muscle. Its contraction is the second etiologic factor in the production of torsion. Torsions of the left testis are predominately clockwise while those of the right are counterclockwise. In some instances the epididymis and testis are joined by a mesentery sufficiently long to allow rotation and strangulation of its blood supply (*4*). Once torsion is established there are two possible terminations if prompt surgical treatment is not given: (*a*) spontaneous detorsion which occurs often enough to provide a suggestive point in diagnosis; and (*b*) hemorrhagic infarction resulting either in necrosis or fibrosis of the testis. Spontaneous detorsion is illustrated by the following case.

Case 3.—A 20-year-old man was admitted complaining of severe pain in the left testis and groin and nausea of about 1 hour's duration. There had been two similar transient episodes in the preceding 2 days. The testis was acutely tender and drawn up against the pubis. En route to the ward, the pain spontaneously subsided, and local findings the following morning were limited to moderate tenderness and increased tension of the affected testis. Both testes were unusually mobile. There was a history of at least one prior similar episode on the other side. A diagnosis of spontaneous detorsion of the left testis was made. On surgical exploration a typical bell-clapperlike deformity was demonstrated. Bilateral fixation was accomplished by excising the parietal tunica vaginalis and suturing the lower pole of the epididymis in its normal posteromedian position.

SYMPTOMS

With the onset of torsion, the chief symptom is acute severe pain in the testis or groin. Typically, the onset is sudden, following strain or slight and inconsequential trauma. The onset of pain has occurred during sleep. The severity of the pain depends on the completeness of the twisting and it may disappear as a result of spontaneous detorsion. This occurs with such frequency that a history of preceding similar attacks terminating spontaneously may be considered suggestive of torsion of the spermatic cord. (See cases 1 and 3.) Nausea, vomiting, and sometimes shock may be present. Usually, there is no temperature elevation and an important point in differential diagnosis is the absence of leukocytosis early in the course. Normal urine, prostate, and seminal vesicles in the presence of the preceding symptoms is indicative of torsion, but there is nothing to prevent torsion from occurring in a man with an infected prostate (*2*).

LOCAL FINDINGS

The affected testis is usually drawn up to the upper scrotum or inguinal region. There is extreme tenderness. This may be so acute that adequate examination is impossible. Unless the testis has rotated through 360°, the epididymis, normally in a posteromedian position, will be abnormally placed. Elevation of the testis causes an increase in pain, a characteristic and almost diagnostic sign (*5*). Edema occurs rapidly and there is nearly always an accumulation of fluid within the tunica vaginalis. In the early stages this is serous but later it becomes serosanguineous.

DIFFERENTIAL DIAGNOSIS

The principal condition that may cause confusion in the diagnosis of torsion of the spermatic cord is acute epididymitis, in which the onset is more gradual, there is early leukocytosis, there is usually some elevation of the temperature, the enlarged epididymis is usually palpable in a normal position, and elevation tends to relieve the distress.

Similar findings are present in acute epididymo-orchitis, but the symptoms are more fulminating. In primary acute orchitis the cord structures are usually normal. Strangulated hernia may simulate the rare extravaginal torsion. Differential diagnosis is not, however, difficult except in the presence of cryptorchism. Vomiting is more frequent in cases of strangulated hernia.

TREATMENT

The treatment of this condition is always surgical. If detorsion is accomplished by manipulation, fixation of the involved testis and the opposite symptomless side is mandatory since the underlying congenital anomaly is usually bilateral. Adequate fixation is easily accomplished by excision of the parietal tunica vaginalis as performed in the usual hydrocelectomy. Spinal or local anesthesia is preferable.

When a reasonable doubt exists, scrotal exploration should be performed. The following case is illustrative.

Case 4.—On 9 June 1947, an 18-year-old man was admitted 30 minutes after the onset of symptoms. He had recently been treated in this hospital for multiple urethral strictures, chronic urethritis, and cystitis. He had awakened with excruciating pain in the right testis, and had vomited once. He appeared acutely ill, and despite a normal temperature his leukocyte count was 14,000. His right scrotum was red and mildly edematous. His right testis was drawn upward to the external ring and because of severe pain, even after an injection of morphine, adequate local examination was impossible. Despite the known urinary tract infection, immediate exploration was performed under spinal anesthesia. On opening the tunica vaginalis, 4 cc. of smoky amber fluid were removed. A blue, discolored testis and epididymis were lying free within the parietal tunica vaginalis, and extreme torsion of the spermatic cord was present. The torsion was corrected, and within 5 minutes the testis resumed its normal color. The parietal tunica vaginalis was excised, with fixation of the testis to the scrotal sac; a two-layer closure was performed without drainage, and convalescence was uneventful. Subsequently, the left scrotum was explored, revealing a free-lying testis and epididymis, with high investment of the cord, constituting the typical bell-clapperlike deformity. The patient was observed for several months and there was no atrophy of the right testis.

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Primary Bronchogenic Carcinoma

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PRIMARY carcinoma of the lung is a curable disease if the diagnosis is made sufficiently early and if complete surgical removal is performed without undue delay. Since Evarts Graham performed the first successful pneumonectomy for carcinoma of the lung in 1933 the safe surgical technique for pneumonectomy has far surpassed the clinical advances in the early diagnosis of this lesion (*1*). Since 1933 several hundred successful pneumonectomies have been performed for cancer of the lung in this country. Thanks to the rapid improvement in endotracheal anesthesia, to whole blood transfusions, antibiotics, and the appreciation of the pulmonary physiology concerned in the pre- and post-operative care of these patients, pneumonectomy has become rather commonplace. We hope for further advances in this field of surgery, but are primarily concerned with the early diagnosis of this dreaded disease. Cancer of the lung comprises from 8 to 15 percent of all cancers in man. It therefore behooves all members of our profession to keep the possibility of this disease constantly in mind, and to exhaust all diagnostic aids to account for unexplained abnormal roentgenographic findings in the thorax associated or unassociated with symptoms.

This article analyzes the recent experience in the diagnosis and treatment of bronchogenic carcinoma at this hospital. In the military service we probably see a larger percent of young men with malignant disease than is ordinarily seen in civilian practice. In the past 5 years we have not encountered cancer of the lung in a female patient. Ninety percent of our admissions have been men. Between 1 January 1944 and 31 December 1948, 91,295 patients were admitted to this hospital. Ninety-one had carcinoma of the lung, proved by histologic examination. The apparent or actual increase in the incidence of this disease is revealed by the fact that of the deaths in this hospital from 1921 to 1940 cancer of the lung was found at autopsy in 27 as compared

[1] Fitzsimons General Hospital, Denver, Colo.

to 55 in the period from 1 January 1944 to 31 December 1948. The ages in this series varied from 22 to 76 years. Sixty-two percent were under 50 years of age and 8 percent were between the ages of 22 and 30 years. Eighty-five were white, five were Negroes, and one was Japanese.

Although the symptoms of primary carcinoma of the lung may be quite variable, most patients present a characteristic history. Initially, the symptoms resemble those of inflammation and depend on the size and location of the tumor as well as the degree of ulceration and obstruction of the bronchus. Seventy percent complained of cough, 55 percent had pain in the chest and weight loss at the time of admission, and 25 percent had hemoptysis. Of these 4 most prevalent symptoms of the disease, cough was the most common initial symptom. In nine patients the duration was less than 30 days and in 26 percent the presenting symptoms were of not over 90-day duration. In 14 patients the lesion was discovered by means of a routine roentgenogram of the chest. Seven of these patients were asymptomatic and five had already reached the inoperable stage. These data emphasize the necessity for immediate and thorough clinical study of patients with suggestive symptoms or findings and the desirability of routine roentgenograms of the chest.

Positive physical findings were more variable than the symptoms. Physical examinations of the chest were negative in 29 patients. Positive findings included various combinations of inspiratory and expiratory sibilant râles, fine to coarse râles, decreased expansion of the involved hemithorax and dullness over the suspected area. It was frequently noted that a relatively small tumor that occluded a main bronchus would give physical findings suggestive of atelectasis or pneumonia, while a peripherally located lesion of greater size that did not obstruct a main bronchus or invade the pleura would produce relatively few physical signs. The less frequent signs of cavitary disease were suggestive of abscess formation complicating the obstructing lesion. It is important to palpate for metastatic peripheral lymph nodes that may occasionally be found in the axillary, supraclavicular, and cervical regions. The involvement of such nodes indicates inoperability. The extent of the atelectasis or pneumonitis is no criterion of the size of the tumor: it generally exceeded the size of the neoplasm.

The late diagnosis of this disease can often be attributed to the insidious development and absence of symptoms in a small bronchial or peripheral pulmonary neoplasm. The patient or the physician often mistakes the carcinoma for pulmonary tuberculosis, virus pneu-

monia, bronchitis, asthma, bronchiectasis, or a chest cold, causing unnecessary delay in establishing the true diagnosis. Often temporary improvement is seen when the bronchial obstruction is intermittent or when antibiotics are employed with temporary abatement of complicating symptoms. These factors often add to the delay in arriving at the correct diagnosis. Jones (*2*) states that "clinical improvement following antibiotic or chemotherapy without complete roentgenographic clearing of a bronchopulmonary lesion in an adult is indicative of at least a tentative diagnosis of primary bronchiogenic new growth until proved otherwise." We strongly concur in this statement. The most important factor in the early diagnosis of this disease is for the physician to require roentgenographic study of the chest in patients with chest symptoms and to demand surgical exploration for unexplained abnormal roentgenographic findings. A history of previous pulmonary disease is of interest but of no particular diagnostic significance. Studies relative to smoking among patients indicate it to be a factor in this disease. The diagnostic aids employed in this study included (*a*) roentgenography (routine and special projection roentgenograms of the chest, fluoroscopy, tomograms, bronchograms, and studies for bone metastasis); (*b*) physical examination; (*c*) bronchoscopy;[2] (*d*) sputum and bronchial secretion studies for tumor cells; (*e*) biopsy of a specimen from the peripheral lymph nodes; (*f*) study of pleural fluid for tumor cells; and (*g*) exploratory thoractomy. Table 1 indicates the initial or early clinical diagnoses made in our series and table 2 indicates the particular method by which the true diagnosis was accomplished. The roentgenographic appearance of bronchogenic carcinoma has no distinctive characteristics. The finding of abnormalities is, therefore, an indication that complete clinical investigation is urgently required. In some cases this may include exploratory thoracotomy (figs. 1, 2, 3, and 4).

TABLE 1.—*Initial clinical diagnoses in 91 patients with carcinoma of the lung*

Initial clinical diagnosis	*Number of patients*	*Initial clinical diagnosis*	*Number of patients*
Carcinoma of the lung	25	Atelectasis	2
Undiagnosed pulmonary disease	22	Pleural effusion	2
Tuberculosis	11	Neurofibroma	1
Carcinoma, primary, site unknown	9	Lobar pneumonia	1
Bronchiectasis	6	Pulmonary cyst	1
Atypical pneumonia	3	Mediastinal tumor	1
Lung abscess	3		
Asthma	4	Total	91

[2] This procedure may yield important information although the actual tumor may not be visualized. Narrowing, distortion, and fixation of bronchi offer aid in determining the nature of the pulmonary process and may assist in the evaluation of operability.

TABLE 2.—*Means by which true diagnosis was arrived at in 62 of 91 patients with carcinoma of the lung* [1]

	Number of patients
Biopsy of specimen removed bronchoscopically	38
Biopsy of specimen of peripheral lymph nodes, mediastinal lymph node, or chest wall	11
Biopsy of specimen of lung at thoracotomy or lobectomy	8
Malignant cells demonstrated in pleural effusion	1
Malignant cells demonstrated in sputum and bronchial secretion	4
Total	62

[1] The remainder were diagnosed at autopsy.

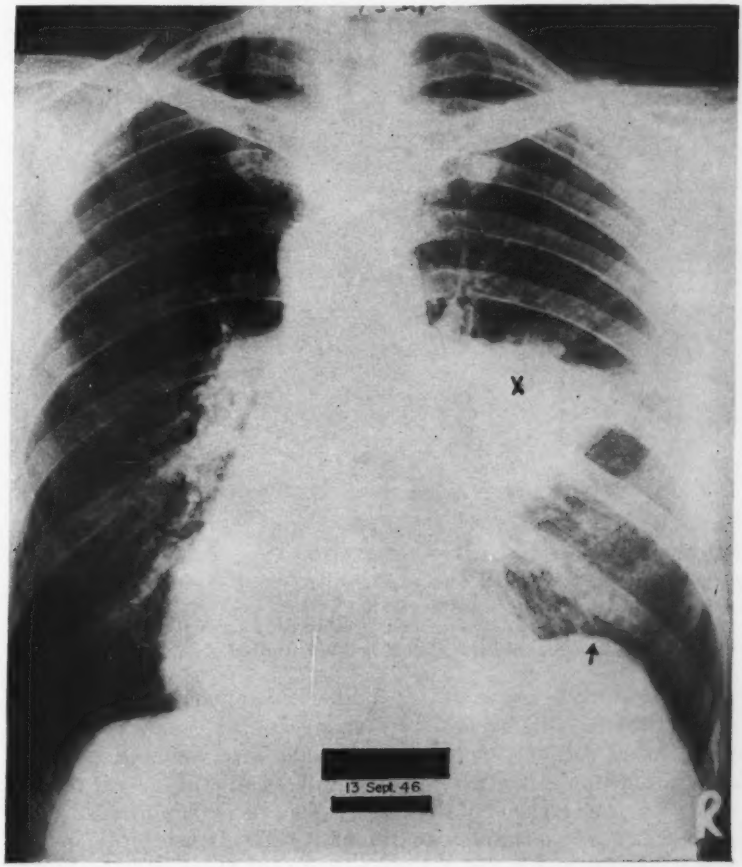

Figure 1.—Roentgenogram of chest of 47-year-old man with symptoms of 4 months' duration. The X marks a bronchogenic carcinoma. The arrow indicates what is probably an elevation of the diaphragm. The right lower lobe of the lung was removed and the patient was alive 3 years later.

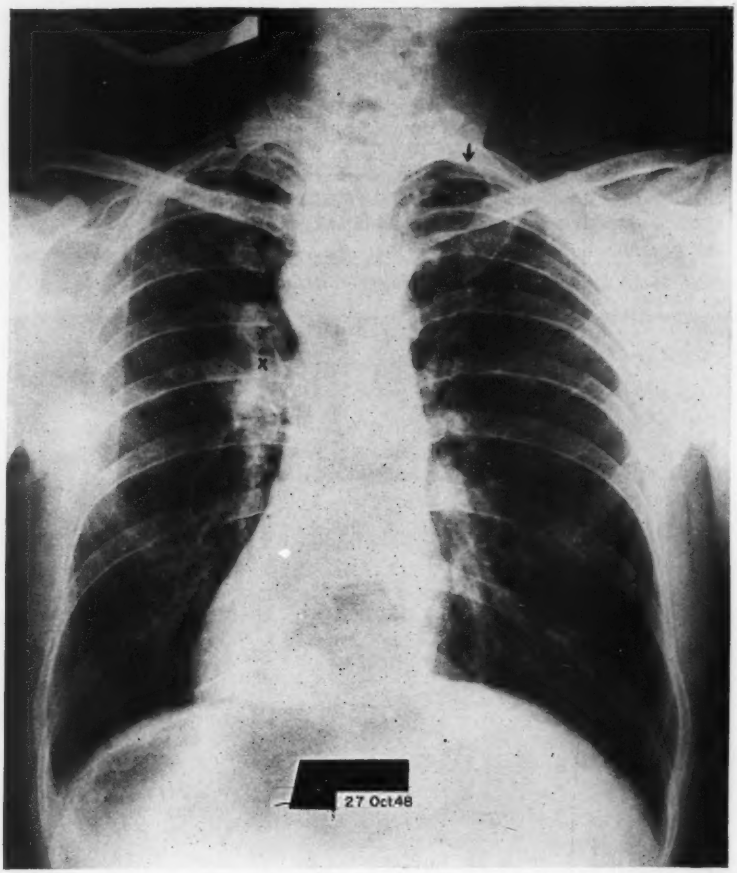

Figure 2.—Roentgenogram of chest of 53-year-old man with symptoms of 2 years' duration. The X marks a bronchogenic carcinoma. The arrows indicate probable pleural thickening. Biopsy showed evidence of carcinoma of the lung. A palliative pneumonectomy of the left lung was performed.

In attempting to arrive at a feasible method of management of carcinoma of the lung we have adopted these criteria. *First*, surgical excision offers the only hope of permanent cure. *Second*, surgical excision offers the best means of affording palliation in patients in whom complete removal of the tumor cannot be accomplished, if there is no evidence of metastases to distant organs. Ochsner (*3*) and his associates have stated that "70 percent of the resections were considered palliative rather than curative since the lesions had extended beyond the confines of the lung. Palliative resections are considered justifiable because the risk is not excessive, the patient's remaining

span of life is more comfortable, and the average survival period is increased." Our experience has been similar and we explore all patients in whom the diagnosis of cancer of the lung has been established who do not have (*a*) involvement of the tracheal wall, (*b*) metastatic lesions to distant nodes and organs, (*c*) malignant cells in the pleural fluid, and (*d*) conditions that preclude operative intervention such as severe cardiac or renal disease.

Radiation therapy has been used in those patients who were inoperable; it has been of doubtful value. In 22 of our patients the tumor

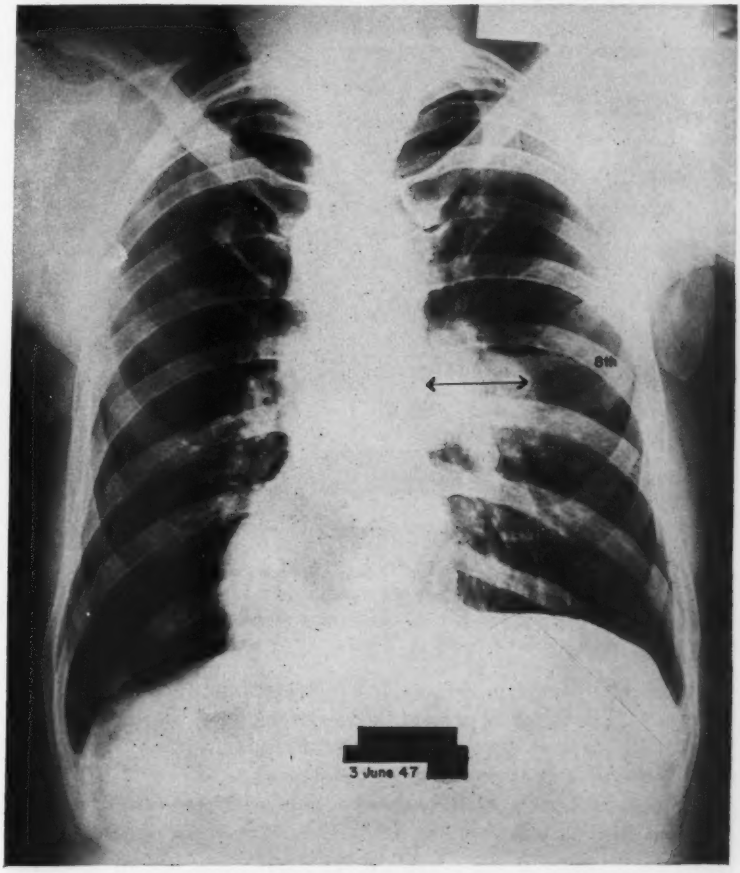

Figure 3.—Roentgenogram of chest of 57-year-old man with no symptoms. The carcinoma in his right lung was discovered by routine roentgenogram. The arrows indicate the site of the lesion. He was alive and working 2 years and 9 months after pneumonectomy of the right lung. The numbers identify ribs.

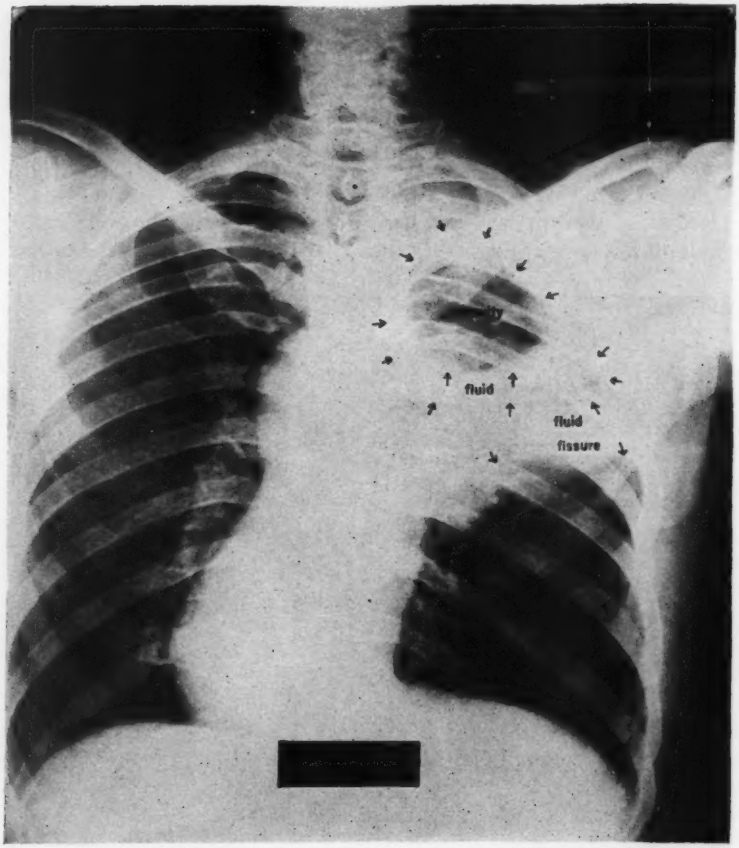

Figure 4.—Roentgenogram of chest of 53-year-old man with symptoms of 9 months' duration. A large cavity is seen in the right upper lobe of the lung. The arrows indicate the site of the lesion. An exploratory thoracotomy was performed but the tumor could not be removed.

was removed by pneumonectomy, in 6 by lobectomy, and in 1 by partial lobectomy. In about 50 percent the resections were considered palliative. There were 3 operative deaths. Four of the patients in this series were alive 2½ years or more following operation. Ochsner has shown that 25.9 percent of the patients survive 2 years after resection and that such patients have an excellent chance of 5-year survival.

CASE REPORTS

Case 1.—A 41-year-old officer was admitted to this hospital on 9 October 1947 with a diagnosis of pleuritis, chronic, right, serofibrinous, tuberculous. He had been in good health until March at which time he developed a slight nonproduc-

tive cough, chills, and night sweats. A roentgenogram of the chest revealed fluid in the right pleural space. He was treated with antibiotics and improved. He was returned to duty at his own request in April and was told that the fluid in his chest would absorb (figs. 5 and 6). He was asymptomatic for about 2 months when chills, fever, and night sweats recurred and he had a productive cough. He was admitted to another hospital where 50 cc. of bloody purulent fluid were obtained from the right pleural space by thoracentesis. The sputum was negative for tubercle bacilli and a roentgenogram of the chest revealed the pleural effusion to be increasing. The treatment consisted of bed rest. The patient grew rapidly worse. The clinical impression was pulmonary tuberculosis, moderately advanced, bilateral, with effusion in the right pleural space. Soon after admission he had symptoms of an obstructive jaundice. He was transferred to this hospital on 9 October. On 31 October bronchoscopy revealed a mass in

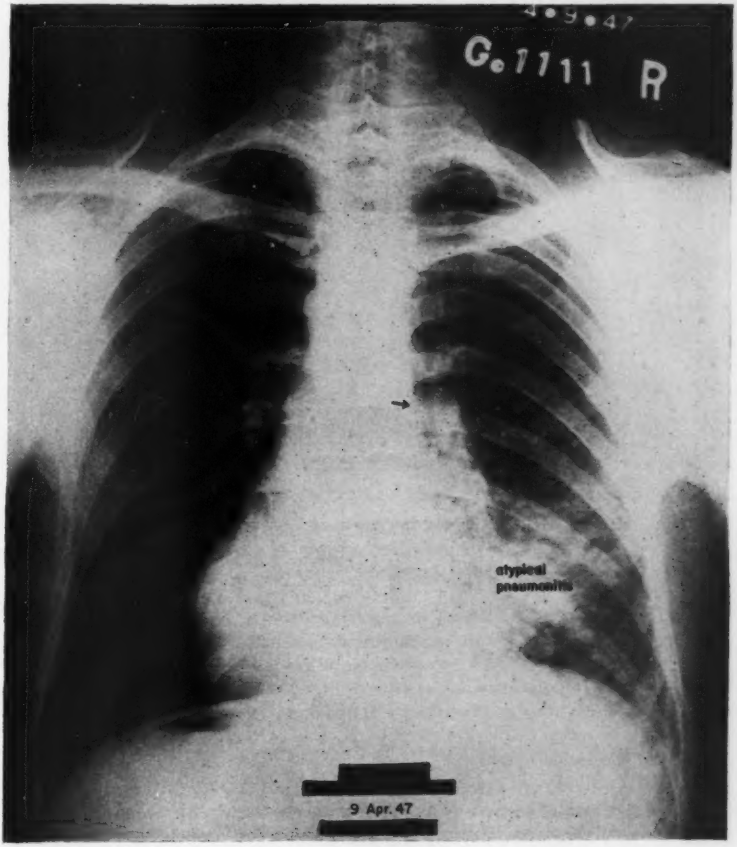

Figure 5.—Case 1. Roentgenogram of chest. The arrow indicates the site of the bronchogenic carcinoma. The lesion marked "atypical pneumonitis" warranted complete investigation. The patient died 8 months later of carcinoma of the right lung.

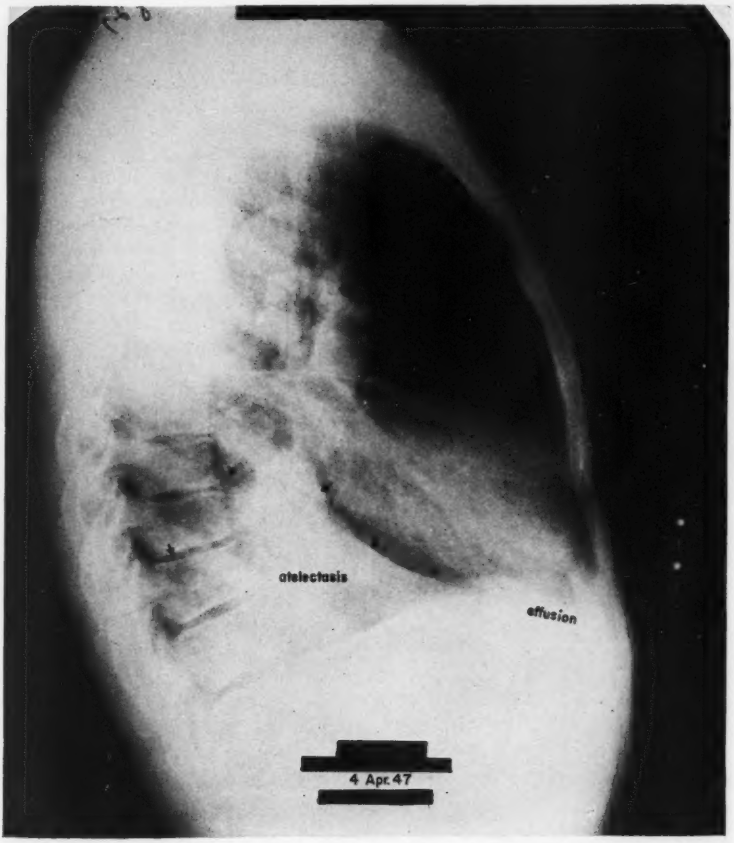

Figure 6.—Case 1. This roentgenogram shows the importance of a lateral projection as an aid in diagnosis. The atelectasis warranted complete investigation. The arrows indicate the site of the lesion.

the right main bronchus. Biopsy of a specimen taken from this mass revealed a carcinoma and a specimen of a subcutaneous metastatic lesion of the right chest wall revealed a similar type of carcinoma. The patient died on 1 December. The post-mortem diagnosis was carcinoma, bronchogenic, undifferentiated, right, with metastasis to hilar and paratracheal nodes, adrenals, right kidney, pancreas, and brain. A proper investigation 6 months earlier might have permitted removal of the lesion and cure.

Case 2.—A 47-year-old veteran had been well until 1943 when he had a severe chest cold from which he never completely recovered. After a 2-month hospitalization he was discharged from the Army because of bronchitis. There were three subsequent admissions to hospitals for bronchitis. In December 1945 he was admitted to this hospital with pneumonia which, except for a small area

in the right lung, responded to penicillin therapy. He was discharged within 2 weeks and continued to work but was bothered by malaise, weakness, and cough productive of foul sputum. A roentgenogram of the chest was made at the request of the out-patient department in January 1946 (fig. 7). In September 1947 he had hemoptysis and was readmitted to this hospital. A roentgenogram of the chest revealed a demarcated, lobulated density in the midportion of the right lung (fig. 8). Bronchoscopy showed an obstructive lesion of the right lower lobe bronchus. Microscopic examination of a specimen of the mass disclosed bronchogenic carcinoma. A right pneumonectomy was performed on 23 September. He died on 7 December 1947. A more complete study in January 1946 might have revealed the true nature of this lesion.

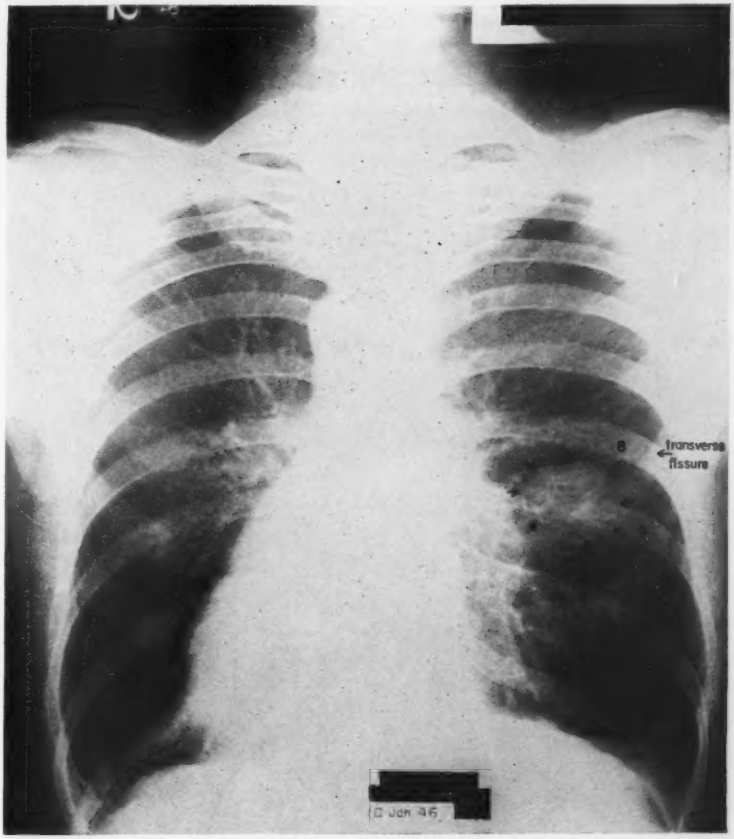

Figure 7.—Case 2. Roentgenogram of chest. The lesion in the right lung indicated by arrows warranted complete investigation. Numbers identify ribs. The patient died 23 months later of carcinoma of the right lung.

TABLE 3.—*Histopathologic classification of 91 cases of carcinoma of the lung*

Classification	*Number of cases*
Squamous cell	45
Adenocarcinoma	19
Undifferentiated	19
Miscellaneous:	
Gelatinous adenocarcinoma	1
Adeno-alveolar	3
Mixed adenocarcinoma and squamous	1
Mixed undifferentiated and squamous	1
Mixed anaplastic and squamous	1
Type undetermined	1
Total	91

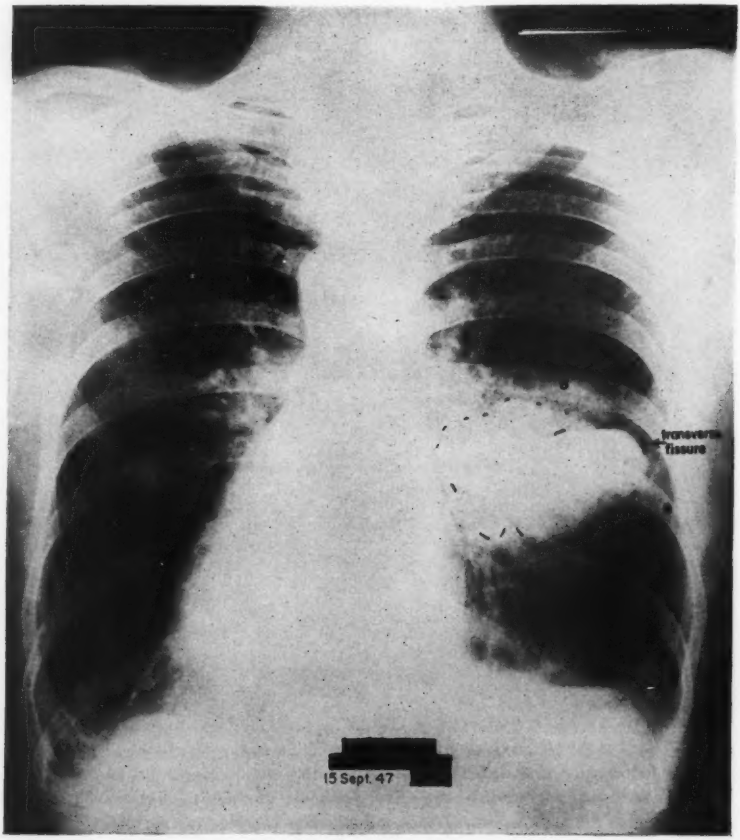

Figure 8.—Case 2. Later view of same lung taken 2½ months before death. Numbers identify ribs.

All bronchogenic carcinomas are highly malignant. The histopathologic classification in this series is shown in table 3. At no time did microscopic study of the tissue and the histopathologic classification influence the operative treatment if a patient was judged operable from a clinical standpoint.

SUMMARY

Pulmonary cancer is now as common as any tumor involving the internal organs in male patients. The disease is believed to be increasing in frequency. The most common symptoms are cough, chest pain, weight loss, and hemoptysis, and patients often present a history pattern suggestive of this disease. Early diagnosis and surgical exploration may save or prolong life. Four patients in the series of 91 patients here reported have survived longer than 2½ years after complete or partial surgical removal of the tumor. Palliative resection of the lesion is recommended.

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The Ante-Mortem Diagnosis of Secondary Tumors of the Heart

Report of Four Cases

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SECONDARY tumors of the heart or metastasis to the heart have been considered rare, and various writers have reported the incidence as varying from 0.28 (*1*) (*2*) to 10.9 percent (*3*). Brick and Greenfield (*4*) in reporting reticulum cell sarcoma with cardiac metastasis, made an extensive review of the literature through 1946. From various surveys of autopsies from leading medical centers, they concluded that the frequency of cardiac involvement varies from 0.03 to 1.4 percent of the total number of autopsies and from 1.0 to 10.9 percent of the total number of cancers. They further noted that up to the time of writing their article, a total of 22 cases of tumor of the heart had been diagnosed ante mortem; of these tumors, 4 were primary (*4*) (*5*) (*6*). Since that report, Blumenthal and Peterson (*7*) reported the ante-mortem diagnosis of metastatic carcinoma of the heart secondary to a carcinoma of the cecum. A case of constriction of the pericardial sac by a neoplasm secondary to bronchogenic carcinoma was reported by Fischer (*8*). Ritz (*9*) reported a case of metastatic tumor of the heart from malignant melanoma, in which ante-mortem diagnosis was made by cell block of pericardial fluid.

In a review of 1,815 autopsies at the U. S. Naval Hospital, Philadelphia, Pa., from 1943 to 1949, 455 cases of malignant tumors were found. Of these, 38 or 8.35 percent were found to have secondary involvement of the heart. In 4 or 10.5 percent an ante-mortem diagnosis was made histologically or else tentatively diagnosed as the cause of cardiac signs and symptoms before death and confirmed by autopsy.

CASE REPORTS

Case 1.—G. A. L., a 68-year-old white man, was admitted to the hospital on 21 April 1947 complaining of a mass in the right axilla which had been found 10 days prior to admission.

Past history.—He had had occasional episodes of anorexia and dull aching pain in the right upper quadrant of the abdomen and black stools and constipation over a period of 9 years. Four years prior to admission a mole on his back had been cauterized without recurrence. Past history was negative for cardiac disease or symptoms. His best weight was 180 pounds, in 1931.

Physical examination.—The patient weighed 134 pounds, his blood pressure was 160/80 and the pulse rate 60 per minute. A firm, nontender, lobulated mass about 6 cm. in diameter was present in the right axillary space, seemingly attached to the pectoralis muscles. The heart examination revealed bigeminal rhythm. A systolic murmur was heard best at the apex, fading toward the base. The rest of the examination was essentially normal.

Laboratory data.—Urinalysis and red and white blood cell counts were normal; hemoglobin, 11 gm.

Roentgenographic examination.—Roentgenograms showed a duodenal ulcer with some contraction deformity. Barium enema was negative. A chest roentgenogram showed increased bronchovesicular markings.

Electrocardiographic and microscopic examinations.—On 22 April 1947 an electrocardiogram revealed a rate of 60 per min. with sinus arrhythmia and sinus arrest. PR interval was 0.17 sec.; QRS was 0.08; the Q-waves, 1 mm. deep in leads 2 and 3. S-T segment was normal.

An electrocardiogram on 8 May 1947 showed complete heart block with the PR interval varying from 0.16 to 0.23 second. Every third P-wave, QRS complex, and T-wave were dropped. The S-T segment became isoelectric in leads 1, 2, and 3.

On 15 May 1947, under local anesthesia, a biopsy specimen was removed from the right axillary mass. The microscopic appearance was that of undifferentiated sarcoma compatible with malignant melanoma.

An electrocardiogram on 18 May 1947 showed a continued block and no change from the record of 8 May 1947.

Tentative diagnosis.—Secondary neoplasm of myocardium.

On 10 June 1947, the right axillary nodes were resected and the microscopic examination showed an undifferentiated sarcoma compatible with malignant melanoma.

Out-patient course and return to hospital.—The patient left the hospital on 18 June 1947 only to be readmitted 12 September 1947 with widespread pulmonary metastasis. He then had bilateral pleural effusion, progressive chest pain on slight exertion, dyspnea, orthopnea, and ankle edema. Cardiac examination revealed bigeminal rhythm and a murmur similar to that noted on previous admission. Blood pressure was 185/90.

A low fluid intake, salt-free diet, and digitalis were prescribed. His course was downhill and he died 28 September 1947.

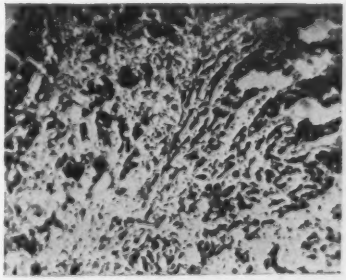

Figure 1.—Case 1. Low-power magnification showing the neoplasm invading the myocardium in the region of the atrioventricular node.

Autopsy.—The autopsy showed malignant melanoma of the right axillary region with metastases to the lungs, liver, pancreas, and thyroid. A chronic duodenal ulcer was present. The heart weighed 330 gm. and was normal in contour. The major vessels and coronary arteries were patent. On sectioning, two metastatic tumor nodules were observed, both approximately 1 to 2 cm. in diameter and located at the atrioventricular junction on the right side. The right ventricular wall measured 4 mm., the left 14 mm. in thickness. The valve leaflets were slightly thickened, the chordae tendineae and papillary muscles were not unusual.

Tumor nodules were found in the atrioventricular node area. Upon microscopic examination these were typical of malignant melanoma, showing evidence of infiltration into the surrounding myocardium.

Case 2.—H. H. C., a 52-year-old white man, was first admitted to the hospital in November 1944, complaining of sharp, steady, and nonthrobbing pain in the left thorax and arm which began in 1942. His family and past histories were noncontributory.

Physical examination.—Examination revealed coarse rhonchi, inspiratory and expiratory râles over both lung fields. On percussion, the mediastinum was found to be widened and the heart to be enlarged. Frequent extrasystoles were audible. Blood pressure, right, 130/90; left, 120/60.

Roentgenographic examination.—A chest roentgenogram revealed a very large, somewhat lobulated area of increased density protruding from the left hilum to the outer fourth of the left lung field. The heart and mediastinum were displaced to the right and the trachea and esophagus were displaced posteriorly.

Laboratory data.—Red and white blood cell counts were normal; hemoglobin, 12.5 gm. The blood Kahn test was negative. Urinalysis was negative.

Electrocardiographic examinations.—An electrocardiogram revealed a rate of 108 per min. and extrasystoles. P-R interval was 0.18 sec.; QRS complex, 0.06 sec. RS-T segment was isoelectric. The T-waves were normal.

Hospital course.—In March 1946, a thoracotomy was performed and what was thought to be an inoperable tumor extending into the pericardial cavity was found. The patient was discharged after convalescence and readmitted in October 1946. At this time, dyspnea and chest pain were more severe. A roentgenogram of the chest revealed little change in tumor density. In November 1946, via an anterior thoracotomy, partial removal of the mass was performed. Following this surgery the patient died.

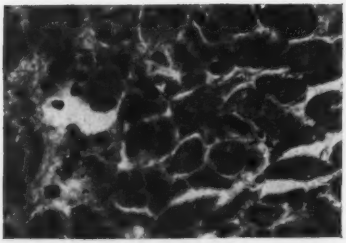

Figure 2.—Case 2. A high-power magnification showing the bronchial adenoma in the myocardium with infiltrative fingers of neoplastic tissue surrounding cardiac muscle.

Autopsy.—Post-mortem examination revealed a solid tumor filling a major portion of the mediastinum and a major portion of the left lung. The resected specimen was filled with multiple lobulations of white solid tumor. A residual pyelonephritis with nephrotic changes was present.

The heart weighed 465 gm. The pericardium was rough, dull, and showed involvement by direct extension

of the mediastinal tumor mass. The ventricles were slightly hypertrophied and there was slight thickening of the mitral leaflets but otherwise the heart was grossly normal.

Microscopic examinations proved the tumor to be a bronchial adenoma. A focal site of neoplastic tissue identical with the lung sections was observed in the left ventricle. Infiltration was noted about the ill-defined margins of the neoplastic tissue.

Case 3.—W. G. G., a 57-year-old white man, was admitted on 6 May 1946 complaining of weakness, dyspnea after walking the distance of one-half block, weight loss of 13 pounds, and abdominal pain of 2-month duration. His general health had been good prior to his present illness.

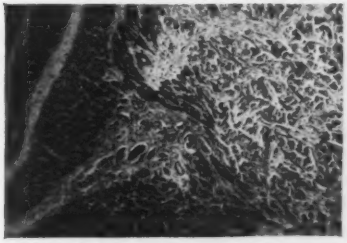

Figure 3.—Case 3. Low-power magnification showing the squamous cell carcinoma invading the surrounding myocardium and extending along the fibrous septi.

Physical examination.—On admission, his pulse rate was 108 and blood pressure, 160/100. The heart showed regular rhythm and no murmurs or enlargement. The neck veins were noticeably distended. The liver was palpable at the right costal margin. No peripheral edema was present.

Laboratory, roentgenographic, and microscopic data.—Red blood cells, 3,100,000; white blood cells, 15,100. Hemoglobin was 8.5 gm. Sedimentation rate was 35 mm./60 min. Roentgenograms were not significant. A biopsy of a specimen from a mass in the left lower lobe bronchus revealed squamous cell carcinoma.

Electrocardiographic examination.—An electrocardiogram taken 10 May 1946 revealed a rate of 92 per min. with normal rhythm. P–R interval, 0.14 sec. The QRS, 0.08 sec. duration with low voltage and slurring in the limb leads. The S–T segment was isoelectric. The T-waves were flattened in lead 2 and inverted in lead 4.

Course and diagnosis.—His course was downhill with evidence of cardiac decompensation. His temperature varied from 99° to 102° F. In light of these findings, a tentative diagnosis of secondary carcinoma of the heart was made. He died on 2 June 1946.

Autopsy.—The post-mortem examination revealed a primary squamous cell carcinoma of the lower lobe of the left lung with superimposed bronchopneumonia and multiple small lung abscesses. Secondary carcinoma of the squamous cell type was found in the liver and kidneys. A small aneurysm of the abdominal aorta and a moderate degree of atherosclerosis of the aorta were found.

The heart weighed 430 gm. The major vessels were patent. The epicardium of the anterior surfaces of the right and left ventricles was covered with a shaggy, granular, yellowish brown fibrinous exudate. The valves and endocardium were grossly normal. The left ventricular wall measured 20 mm. in thickness. The interventricular septum revealed small, white, firm, solid flecks scattered diffusely throughout the myocardium. Microscopically, the interventricular septum was found to be infiltrated with secondary squamous cell carcinoma; scattered round-cell infiltration was present about the margins of the tumor.

Case 4.—B. J. P., a 22-year-old white man, was admitted to the U. S. Naval Hospital, Philadelphia, Pa., on 7 July 1948. In April 1947 he had been hospitalized at Walter Reed Hospital where biopsy of a specimen of a mediastinal tumor was reported as being a cavernous hemangioma. However, on review of the slides it was subsequently thought to be malignant teratoma.

At the time of entry into this hospital, he complained of severe substernal pain of 5-week duration with extreme dyspnea of 2-week duration. He was unable to lie flat in bed and had insomnia for this reason. He complained of coughing and nausea and had lost 12 pounds in the month prior to admission.

Physical examination.—His pulse rate was 96 per minute; respiratory rate, 18 per minute. Temperature and blood pressure were normal. The chest showed dullness on the right side from 3 centimeters above the tip of the scapula downward and there was impairment of breath sounds. The neck veins were greatly distended. A soft mass was felt in the left supraclavicular region. The liver was enlarged, soft, and tender.

Roentgenographic examination.—A chest roentgenogram showed pleural effusion on the right side and an operative defect of the left sixth rib posteriorly. Obliteration of the left costophrenic angle was also seen.

Hospital course.—He became increasingly dyspneic. Thoracentesis gave partial relief and examination of the fluid showed no tumor cells.

After 16 July 1948, his temperature remained about 101° F. orally, daily. Despite repeated thoracentesis, his dyspnea and right-side heart failure continued. The fluid obtained at thoracentesis on 20 August 1948 was found to contain neoplastic cells (fig. 4).

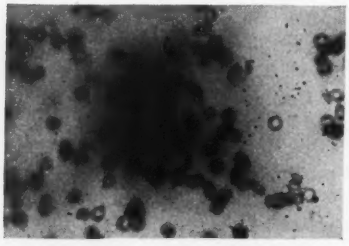

Figure 4.—Case 4. High-power magnification of clumps of neoplastic cells found in the effusion fluid.

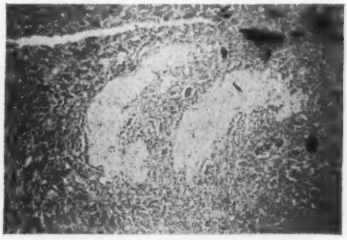

Figure 5.—Case 4. A low-power magnification showing the masses of neoplastic cells isolating bundles of cardiac muscle. Note the pseudoacinar formations in the neoplastic tissue.

Because the pleural effusion was due to a neoplastic lesion, the pericardial effusion was logically attributed to the same factor. Repeat roentgenograms of the chest showed mediastinal infiltration with pericardial involvement.

A biopsy specimen from the left supraclavicular region showed a secondary undifferentiated tumor of a lymph node.

Laboratory studies showed the removed pleural fluid to contain 4 percent solid matter. Repeated cultures of the pleural fluid showed no bacterial growth. The red blood cell count varied between 4.4 and 5.3 million; the hemoglobin from 12.5 to 14.5 grams percent; the white blood cell count from 6,900 to 11,200

with the average differential count showing 76 percent polymorphonuclear neutrophils, 8 percent eosinophils, 2 percent basophils, and 14 percent lymphocytes. Total serum proteins were 4.45 grams percent. The blood Kahn test was negative. A bromsulfalein test with 5 mg. of dye per kilogram revealed 32 percent dye retention in 30 minutes. Sputums were repeatedly negative for acid bacilli. The patient continued to have fever, to lose weight, and became dyspneic. He died 9 October 1948.

Autopsy.—Autopsy was limited to the chest. The pleural cavity on the right side contained 1,250 cc. and the left 1,200 cc. of a bloody coagulative material showing a specific gravity of 1.022. The pericardial sac contained a similar fluid totaling 500 cc. The pleural and pericardial surfaces were studded with white tumor nodules which varied from 4 mm. to 2 cm. in diameter.

The lungs, in addition to tumor extending into the lung parenchyma from the hilar regions, showed multiple zones of atelectasis. The mass weighed 1,250 grams.

The tumor had infiltrated around the great vessels entering and leaving the heart. The heart weighed 175 grams. Upon section, the myocardium was atrophic, the left ventricle measuring 8 mm. in thickness, the right 4 mm. Tumor infiltration into the myocardium extended beneath the pericardium.

DISCUSSION

In case 1, the diagnosis of a melanoma was established prior to death. In this case, the cardiac symptoms and signs occurred after the appearance of the melanoma. It was logical to tentatively consider the pathologic heart changes to be due to a metastatic lesion until ruled out by clinical course or other means.

The diagnosis was confirmed at autopsy; the tumor was so located in the region of the heart that alteration of rhythm would very likely be initiated.

In case 2, surgical observation showed the tumor to extend into the pericardial cavity and when cardiac symptoms occurred it was postulated that myocardial invasion was the likely cause. However, it was not certain that the tumor in the ventricle was responsible for his cardiac condition since the pericardial and pulmonary pathologic changes could well have been the responsible factors.

In case 3, the patient was observed for 27 days. He was known to have a malignancy of the bronchus. His cardiac signs and symptoms were thought to be out of proportion to the degree of arteriosclerosis. The electrocardiogram was of some help in ruling out thrombosis and infarction. With the existing neoplasm and its tendency to metastasize to the myocardium, it was logical to consider the presence of secondary neoplasm of the myocardium in addition to arteriosclerosis. Also considered in the differential diagnosis was mural thrombosis or neoplastic extension via the pulmonary veins. No obstructive phenomenon was demonstrated. The numerous areas of neoplastic infiltration found at autopsy were small and scattered, and conse-

quently these did not alter the electrocardiogram in any appreciable fashion.

In case 4, a diagnosis of pleural involvement by a neoplasm was made on finding neoplastic cells in the pleural effusion and the presence of signs of mediastinal involvement. The exact site of the superior vena cava obstruction was not clear and intra- and extra-pericardial sites were thought to be the best possibility. From the autopsy findings it appeared that both the infiltration of the myocardium and the obstruction of the blood entering and leaving the heart chambers, in addition to the pressure from the pericardial effusion, were factors in the production of his cardiac signs and symptoms.

The cardiac changes which occur following primary and secondary tumors of the heart are similar. No matter which exists, when an infiltrative expanding process is present it produces the same effects.

In an article by Hamilton-Paterson and Castleden (*10*) pseudotumors arising from organization of blood clots and aneurysms, give patterns of cardiac disease not unlike primary sarcoma of the heart. Brick and Greenfield (*4*) emphasized the view of Scott and Garvin (*3*) that patients with known malignant neoplasms who have cardiac failure should be suspected of having secondary neoplastic disease of the heart. This sign alone probably outshines all the other findings, including changes in rate, rhythm, and displacements of the segments in the electrocardiogram.

The literature (*4*) (*11*) (*12*) (*13*) indicates that high-voltage roentgen therapy may prolong the life of the patient as well as relieve the distressing signs and symptoms which may accompany the secondary lesions in the heart.

In the four cases presented the primary lesions were in the bronchus, the skin, and the embryonal tissue of mediastinum. However, the primary lesion may be in any organ; in the majority of cases, the breast and bronchus have been the primary sites. Lung involvement is a common finding when malignant cardiac invasion is present regardless of which organ is primarily involved. The heart may be invaded by a tumor extending along the blood vessels and lymphatics, or by distribution of the neoplastic cells through the coronary artery. Pericardial involvement as well as myocardial involvement is frequent.

Direct extension or lymphatic permeation are the probable routes to the pericardial surfaces. The site of involvement is more important than the extent of involvement in myocardial metastasis, but the extent of involvement seems to be more important in metastatic pericardial lesions.

At this hospital 90 percent of the patients with metastatic lesions of the heart who had no signs or symptoms were unsuspected of having such lesions before autopsy.

The failure to made an ante-mortem diagnosis in cardiac malignancy probably depends on several factors. The symptoms are quite variable and cardiac symptoms may be absent or else sudden as severe heart failure or bizarre arrhythmia may occur. The ample heart reserve, the lack of valvular involvement, and the absence of acute infarction and debility of the patient may not arouse suspicion of a cardiac lesion. Failure of the involved heart may be difficult to detect in patients showing a picture of chronic constrictive pericarditis as reported by Wallace and Logue (*14*), Fischer (*8*), Lisa et al. (*15*). They pointed out that in patients showing evidence of congestive heart failure who are refractory to treatment cardiac tumors should be suspected, especially if there is no obvious cause for cardiac failure.

It is interesting that in our patients the lesions occurred in or extended into the substance of the myocardium. In one patient invasion of the atrioventricular node was demonstrated as the probable cause of arrhythmia. The changes in the electrocardiograms parallel ischemic lesions of the myocardium or extensive scar replacement of the muscle fibers. Mayhaim (*16*) described a secondary cardiac tumor in which the sino-atrial node was destroyed and rhythm was determined by the atrioventricular node.

Positive diagnosis of metastatic tumors of the heart can only be be made on histologic examination of the myocardium. Nevertheless, the possibility of metastasis to the myocardium should be kept in mind. When unexplained cardiac signs and symptoms occur in a patient with a malignant tumor and when little or no cardiac abnormality was previously observed, the ante-mortem diagnosis of secondary tumor of the myocardium can be made with some degree of certainty.

SUMMARY

Secondary tumors of the heart are not rare. During a 6-year period they were noted in 8.35 percent of all necropsies performed on patients who had malignant neoplasm.

Any patient harboring a known malignant neoplasm who shows cardiac signs should be suspected of secondary involvement of the heart.

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Idiopathic Thrombocytopenic Purpura

Splenectomy and Toluidine Blue in Treatment

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PURPURA is a condition in which hemorrhages or ecchymoses occur in the tissues because of an alteration in the capillaries, or the blood, or both. Capillary alteration has been assumed to be due to defects in the vascular endothelium; the capillaries are either unable to contract when injured or else they are unusually permeable. Recently Humble (*1*), employing capillary microscopy, has studied the mechanism of hemorrhage in 17 cases of purpura. Five of these were idiopathic thrombocytopenic purpura and in these he found the mechanism to be the same in all cases. In the arteriolar end of the capillary loop, the part from which tissue fluid normally leaves the vessels he observed a shower of red cells hurled from the vessels. No breach of the blood stream in the capillary was evident nor was the capillary obliterated by the pressure of effused blood. He postulates a selective poisoning of this junction.

Other workers believe that thrombocytopenia may be the result of decreased platelet formation, or increased platelet destruction, or increased requirements of platelets. Any factor in the clotting mechanism may be defective; there may be a deficiency of thromboplastin, prothrombin, calcium, or fibrinogen. Allen and Jacobson (*2*) indicate that purpura may at times result from hyperheparinemia.

CLASSIFICATION

The author prefers Murphy's (*3*) classification of purpura. For the practicing physician it is simple, clear, and workable, and is therefore worth repeating:

1. *Primary purpura (idiopathic, essential).*—The cause is unknown: No associated disease that may be the cause of the purpura is found.

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2. *Secondary purpura.*—Secondary purpura refers to those cases in which another disease is considered to be the cause.

(*a*) Secondary thrombocytopenic purpura in which thrombocytopenia is one of the main features. It is seen in myelophthisic anemia, pernicious anemia, the leukemias, aplastic anemia, and platelet depression from irradiation, radium, or drugs.

(*b*) Secondary purpura without thrombocytopenia. This condition is noted in:

(*1*) Acute infections such as cerebrospinal meningitis, measles, scarlet fever.

(*2*) Toxic or allergic states caused by such agents as quinine, gold salts, barbiturates, mercury, sulfonamides, quinacrine, iodides, arsenicals, salicylic compounds, pertussis vaccine, estradiol benzoate, blood transfusions.

(*3*) Constitutional debility such as chronic nephritis, cancer, syphilis, scurvy and other avitaminoses.

(*4*) Septic infections such as subacute bacterial endocarditis, meningococcemia.

Every effort should be made to distinguish the idiopathic from the secondary variety. This is important because the treatment of the two types is very different. Treatment of secondary purpura resolves itself into the treatment of the underlying disease. For idiopathic thrombocytopenic purpura splenectomy is resorted to. It often cures. This operation, even though it has been performed for the past 33 years, still rests on an empirical basis.

INCIDENCE

In a series of 90 cases (*4*) of idiopathic thrombocytopenic purpura the incidence of females to males was 3:1. It was found most commonly in those under 25 years of age (58.9 percent). In this 27-year study only 2 cases were seen in males over 25 years of age.

PATHOLOGY

The pathology of secondary purpuras varies with that of the underlying disease. In idiopathic purpura there is thrombocytopenia and hemorrhagic manifestations with a paucity of other significant findings. No constant pathologic change is found microscopically. Nickerson and Sunderland (*5*) describe the following changes in the spleen: enlargement and activity of the germinal centers, megakaryocytes in pulp sinuses, neutrophilic and eosinophilic leukocytes increased in splenic pulp sinuses.

DIAGNOSIS

Chief features in diagnosis.—The chief features in diagnosis are:

(*a*) A great reduction of platelets.
(*b*) Prolonged bleeding time.
(*c*) Normal clotting time, but delayed or absent clot retraction.

(*d*) The red and white blood cell counts are normal, except as noted in differential diagnosis.

(*e*) A decreased capillary resistance as shown by the tourniquet test: petechial hemorrhages occur over the entire forearm below the level of the blood pressure cuff.

Differential diagnosis.—This involves the exclusion of all factors known to cause secondary purpura. In idiopathic thrombocytopenic purpura the spleen is occasionally palpable. However, a very large spleen would make one think of leukemia with purpuric manifestations. Purpura with leukopenia would make one think of aplastic anemia or an aleukemic leukemia. A leukocytosis is found in the presence of secondary infections. Anemia, when present, is not out of proportion to the blood lost.

SPLENECTOMY AS TREATMENT

Other than medical management, including repeated transfusions, bed rest, a high-calorie diet, good nursing, symptomatic therapy, removal of focal infection when found, and use of antibiotics when indicated, splenectomy is offered as the sheet anchor of therapy. The impression is that splenectomy is practically infallible.

Haden (*6*) states: "Splenectomy in the acute cases should be done if the response to other treatment is not satisfactory. In chronic cases results are excellent."

Kracke (*7*) states that a recurrence was not observed in 9 years at the Emory University Hospital in a series of 23 patients after splenectomy.

Commenting on splenectomy, Downey (*8*) remarks: "Splenectomy is, therefore, not only a lifesaving but a curative measure in thrombocytopenic purpura which heretofore has been regarded as incurable and accompanied by a high mortality." He reports only one failure in a series of 36 cases (operation successful in 97.4 percent).

It is known that this disease is prone to develop remissions and that the course is so varied that adequate appraisal of any form of therapy will require extended observation. For this reason, both because of the size of the series and the prolonged observation of the cases reported by Elliott (*4*) it would appear that his findings approach a truer approximation of what one can expect from splenectomy. He reports a 27-year follow-up experience. In a total of 64 cases of idiopathic thrombocytopenic purpura there was a successful result in 69 percent following splenectomy. Breaking this down by age groups, it is found that splenectomy was successful in 95.1 percent of the patients under 31 years of age; results were successful in only 42.9 percent of the patients over age 31 years. The reason for the increased failures of splenectomy in those over 31 years of age is not known.

This difference is important in considering prognosis. Patients under 31 years of age have about a 95-percent chance of cure by splenectomy, whereas those 31 years of age and over have only about a 43-percent chance of cure by splenectomy.

The following is a case report of one patient with idiopathic thrombocytopenic purpura treated with splenectomy and toluidine blue.

CASE REPORT

A 19-year-old married white man first noted the onset of purpura of the skin, anorexia, and weakness in June 1947. He entered a naval hospital because of frequent occurrence of purpuric areas over his body, repeated moderate nasal hemorrhages, and splenomegaly. The spleen was barely palpable. There was no history of exposure to chemicals or drugs and no history of recent infection. A diagnosis of purpura hemorrhagica was made and on 17 July 1947 a splenectomy was performed. The postoperative course was uneventful. The hemorrhagic manifestations promptly ceased and on 5 September 1947 he went on convalescent leave.

The patient remained well until 15 September 1947 when he noted general malaise. The next day he noted chills and fever and 2 days later was admitted to this hospital.

Physical examination.—Physical examination revealed a temperature of 102.8° F.; pulse, 110; respiration, 28; blood pressure, 110/60. There was crusted blood about the nares. The mucous membranes were pale. Moderate-sized palpable lymph nodes were present in the neck, left axilla, and both inguinal regions. Examination of the lungs revealed dullness, decreased tactile and vocal fremitus, and decreased breath sounds in the left lower lobe. There were a few pin-point petechiae over the trunk.

Roentgenographic examination.—A chest roentgenogram revealed diffuse mottling with a tendency to follow the bronchovascular markings.

Laboratory findings.—Urine was negative. Peripheral blood: Red blood cell count, 2.8 million; hemoglobin 10 gm.; white blood cell count, 31,500. The differential blood count revealed myelocytes 2, juvenile cells 2, band forms 3, segmented neutrophils 55, lymphocytes 24, monocytes 4. There were 8 normoblasts per 100 white blood cells. Red cells showed moderate achromasia and anisocytosis. Platelets were too few for accurate count. Bleeding time, 14 minutes 20 seconds. Clotting time, 4 minutes 20 seconds. Clot retraction, 0 in 24 hours. Fragility test, normal. Blood Kahn test, negative. Prothrombin time, 95 percent of normal.

Blood chemistry values were within normal limits except for nonprotein nitrogen of 230 mg. per 100 cc. of blood.

Biopsy of sternal marrow revealed count shown in table 1.

Treatment and hospital course.—The patient was treated with penicillin and frequent whole blood transfusions. Petechiae and ecchymoses recurred periodically. Moderate nasopharyngeal bleeding occurred intermittently. He made a slow recovery and on 15 November 1947 had a remission with cessation of his purpuric manifestations and evidence of normal lungs. His blood picture, both peripheral and sternal, remained essentially unchanged except for improvement in red blood cell count and hemoglobin.

TABLE 1.—*Sternal marrow*

Cell	Normal count [1]	Patient's count	Cell	Normal count [1]	Patient's count
Myeloblasts	0.3- 5.0	0.4	Basophils	0.0- 0.7	0
Promyelocytes	1.0- 8.0	1.2	Lymphocytes	3.0-17.0	2.0
Myelocytes		[2] 5.5	Plasma	.0- 2.0	0
Neutrophilic	5.0-19.0		Monocytes	.5- 5.0	0
Eosinophilic	.5- 3.0		Reticulum	.2- 2.0	0
Basophilic	.0- .5		Megakaryocytes	.3- 3.0	.4
Metamyelocytes	13.0-32.0		Pronormoblasts	1.0- 8.0	3.4
Neutrophils	7.0-30.0	64.9	Normoblasts	7.0-32.0	14.6
Eosinophils	.5- 4.0	.6			

[1] See reference (*9*).
[2] Total.

During this remission adrenalin 1:1000 was used as a diagnostic test to determine the presence of an accessory spleen. Before adrenalin was given, the blood cell count was 4.1 million and the platelets 4,170 per cu. mm.; after the administration of 0.4 cc. of adrenalin, the red blood cell count was 4 million and the platelets 48,000 per cu. mm.

The patient remained asymptomatic until 3 January 1948 when he had hematuria, epistaxis, and slight bleeding from the throat and tongue. He received frequent whole blood transfusions. On 2 February 1948 he had severe frontal and temporal headaches assumed to be due to intracranial hemorrhage. At this time his entire body was covered with petechiae. Transfusions were without apparent effect. Toluidine blue, 2 milligrams per kilo body weight, was given intravenously with no effect on the hemorrhagic manifestations. He died 24 hours later. The body was not discolored by use of the dye.

Post-mortem examination.—Autopsy revealed extensive hemorrhage throughout the body. The entire body was covered with multiple petechiae. The nares, mouth, gums, and tongue revealed areas of hemorrhage. There was a recent hemorrhage in the left occipital area and an old hemorrhage in the right posterior frontal region of the brain. The lower lobe of the left lung revealed fairly large areas of hemorrhage. The entire gastrointestinal tract was hemorrhagic. There was hemorrhage into the pelvis of the right kidney and massive hemorrhage from the bladder mucosa. No accessory spleen was found.

There was much to indicate that the lymph nodes had assumed the functions of the spleen. Grossly they were slightly enlarged and reddish purple in color. Microscopic sections revealed the capsule to be intact; the peripheral sinuses were filled with blood cells; the architecture of the lymph glands was preserved; and the lymph follicles showed some endothelial proliferation and hyperplasia of the germinal centers. Throughout the entire lymph node there was considerable red blood cell infiltration and a great number of eosinophils.

TABLE 2

	Spleen	Lymph nodes
Size	Normal or slightly enlarged	Slightly enlarged.
Color	Reddish purple	Reddish purple.
Architecture	Preserved	Preserved.
Capsule	Normal	Normal.
Red blood cells	In pulp sinuses	Filled peripheral sinuses.
Germinal centers	Enlarged	Hyperplastic.
Megakaryocytes	In pulp sinuses [1]	Not described.
Eosinophils	Increased in splenic pulp	Marked number throughout node.

[1] Megakaryocytes are few in number and may be missed unless diligently searched for.

The similarity between the spleen of idiopathic thrombocytopenic purpura as reported by Nickerson and Sunderland (*5*) and the lymph nodes of this patient who had a recurrence after splenectomy is graphically seen in table 2.

TREATMENT WITH ANTIHEPARIN COMPOUNDS

Allen and coworkers (*2*) (*10*), in 1947, reported studies with toluidine blue and protamines in purpuras. They suggested there was an increase of heparinlike substances in the blood and that these agents rendered heparin inactive, thereby controlling capillary permeability. Toluidine blue was used in doses ranging from 1 to 4 mg. per kilo body weight in 250 to 500 cc. of physiologic salt solution given intravenously over a 2-hour period. Their patients usually responded in from 24 to 48 hours. In four of their patients acute or subacute leukemia was present and were thus secondary purpuras; in all they obtained beneficial results. In one of their patients idiopathic thrombocytopenic purpura showed a remission after receiving toluidine blue. After refusing further therapy the other patient with idiopathic purpura died.

Parkin and coworkers (*11*) reported one patient with idiopathic thrombocytopenic purpura treated with protamine sulfate and toluidine blue. Hemorrhagic phenomena continued in spite of administration of 120 mg. protamine sulfate over a period of 4 days and 312 mg. of toluidine blue over an 11-day period. They thought this method of therapy was of no benefit in idiopathic thrombocytopenic purpura. Holoubeck et al. (*12*) have reported their experiences with the use of toluidine blue in the treatment of purpura associated with thrombocytopenia. One of their patients met the criteria of idiopathic thrombocytopenic purpura; the case histories of two others indicated secondary purpura. The patient with idiopathic purpura failed to benefit from toluidine blue therapy. The two patients with secondary purpura promptly responded to toluidine blue. Holoubeck and his coworkers have done toluidine blue titrations on 30 patients with purpuric states associated with thrombocytopenia. In this series they have always found the test positive in leukemias. They believe proper selection of cases extremely important.

Our patient treated with toluidine blue received a single injection according to the method recommended by Allen and coworkers (*10*). He died within 24 hours. Toluidine blue was entirely without effect. After its use the hemorrhagic manifestations did not increase; neither was there any diminution in them. This form of therapy, even when combined with whole blood transfusions, did not prolong life nor did it appear to hasten death. The body was not discolored at time of death.

Antiheparin compounds appear to be of value in secondary purpuras. Their value in idiopathic thrombocytopenic purpura is questionable but they should be employed when more conservative methods of treatment fail to produce improvement. To properly evaluate this method of therapy a larger series of cases will be required. With an accurate test for hyperheparinemia (which can be performed by the average hospital laboratory) idiopathic thrombocytopenic purpura may be narrowed down still further.

Much more study of purpura is required. In time easily applied tests to determine the adequacy of all factors in blood coagulation may be found. The therapy of splenectomy still rests on an empirical basis.

DISCUSSION

All idiopathic purpuras do not respond to splenectomy. Some do not have accessory spleens. Splenectomy is not as successful as the literature indicates it to be. The operation still rests on an empirical basis and why some patients benefit and others do not is not known. Much further study is required to elucidate the problem of purpura.

A rise of the platelet count of 44,000 per cu. mm. after receiving 0.4 cc. of 1:1000 adrenalin is not a positive test for an accessory spleen.

Lahey (*13*) believes that if a purpura fails to respond to splenectomy there is either an accessory spleen or the case is not idiopathic purpura. Splenectomy failed to cure the case reported. No accessory spleen was found at autopsy. The case meets the criteria of idiopathic thrombocytopenic purpura. Failure of splenectomy may be due to blockage of platelets so that they are not released into the general circulation, to the reticulo-endothelial or lymphatic system assuming functions of the spleen, or to other as yet unrecognized cause. With the present knowledge perhaps it would be better to reclassify idiopathic purpuras cured by splenectomy as splenic purpura even though the operation still rests on an empirical basis.

The antiheparin compounds have been most successful in secondary purpuras. A reliable readily performed test for hyperheparinemia would put antiheparin therapy on a rational basis in all purpuras. It failed to benefit the case reported here.

In the case reported there is evidence to indicate the lymph glands had assumed the functions of the spleen.

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Bilateral Circumscribed Pretibial Myxedema

Report of a Case

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IT IS perhaps unfortunate that the term "myxedema" as introduced by Ord in 1878 is so thoroughly entrenched in the literature that it has come to be practically synonymous with hypothyroidism. This is an implication that is not always correct.

Variations in the clinical appearance of myxedema have long been noted. Kreibich (*1*) in 1927 suggested a division of myxedema into three different clinical types as follows: (*a*) The diffuse type, the classical generalized myxedema of hypothyroidism; (*b*) myxedema papulatum; and (*c*) myxedema tuberosum. Pillsbury and Stokes (*2*) proposed a further differentiation of myxedema tuberosum into two distinct subgroups: (*a*) Localized nodular infiltrations—associated with hypothyroidism and of varying location but usually not on the lower extremities; and (*b*) the relatively rare bilateral circumscribed pretibial myxedema. The latter has distinct and constant characteristics.

The syndrome of bilateral circumscribed pretibial myxedema is discussed in this article. A typical case of this fairly uncommon syndrome is reported.

CASE REPORT

H. I. B., a 26-year-old white man, a native of Massachusetts, was admitted to the sick list at Adak, Alaska, on 20 December 1945, with a history of increasing nervousness, irritability, weakness, dysphagia, and tremor of the hands since October 1945. In the 2 months prior to admission he also noted some fullness in his neck and a bulging of the eyes. There was a 20-pound weight loss.

Past medical and familial histories were noncontributory.

Positive physical findings consisted of extreme exophthalmos and a palpably enlarged thyroid with a bruit. Tremor of the hands was evident. A tachycardia of 140 was present, and the blood pressure was 150/90. The heart was slightly enlarged and a systolic apical murmur was heard. The remainder of the physical findings were negative.

Routine laboratory studies were within normal limits. The basal metabolic rate was plus 50 on admission.

On transfer to the U. S. Naval Hospital, Seattle, Wash., he was treated with Lugol's solution; a subtotal thyroidectomy was done on 21 January 1946. The pathologic diagnosis was toxic nodular goiter.

The postoperative course was uneventful. He gained 30 pounds, regaining his normal weight. There was some regression of the exophthalmos as determined by exophthalmometric readings. Reported basal metabolic rates ranged from plus 6 to plus 9.

The patient was discharged May 1946, but was readmitted on 10 March 1947 to the U. S. Naval Hospital, Chelsea, Mass., because of difficulty in lid closure. There had been no recurrence of symptoms.

Figure 1.

Examination on this readmission revealed extreme exophthalmos with slight corneal edema. There was no other change in the physical findings except for the presence of bilateral circumscribed pretibial plaquelike tumors which had not been previously noted. These lesions were firm, discrete, plaquelike ovoid masses which moved with the skin on palpation. The masses seemed to be definitely cutaneous. There was slight inflammation of the overlying skin, and "pigskin" dimpling was evident. The lesions were located in the middle third of the pretibial areas (fig. 1). The right lesion measured 6 cm. longitudinally by 5 cm.; the left, 9 cm. by 6 cm.

These masses were first noted by the patient in May 1946. They were bilateral then and had enlarged rapidly to their present size. There were no symptoms referable to the lesions.

Routine laboratory studies were negative. Blood cholesterol was 208 mg. per 100 cc.; basal metabolic rate was minus 4.

A consultant considered the lesions to be bilateral circumscribed pretibial myxedema. A specimen for biopsy from the left pretibial lesion was removed in March 1947. On incision, a glistening, gelatinous fluid oozed from the wound. Microscopic sections revealed a splitting of the connective tissue of the corium. The epidermis was normal, and there was no evidence of inflammation. The interstitial substance was identified as "mucin."

The course during this second hospitalization was uneventful. There was no change in the appearance of the pretibial lesions. The patient was discharged in April 1947. Subsequent follow-up has not been possible.

DISCUSSION

The importance of the syndrome rests mainly on its rarity and on the fact that the myxedema is consistently pretibial and bilateral and occurs almost invariably in association with thyrotoxicosis.

Bilateral circumscribed pretibial myxedema was apparently not recognized clinically until Watson-William (*3*) reported the first case in 1895 and mentioned another case so recognized by Hektoen. Another case was reported in 1899 (*4*) but the condition was subsequently neglected in the literature until a report of a case by Richter (*5*) in 1927 revived interest. Since then a number of cases have been reported.

Bilateral circumscribed pretibial myxedema is of relatively rare occurrence; only 84 recognizable cases have been found in the literature. However, the incidence is considerably higher than might be supposed if one considers the number of cases unrecognized or unreported. Trotter and Eden (*6*) reported an incidence of 3 percent in their series of thyroid cases. Dunhill (*7*) noted a similar incidence.

Conclusions as to the age and sex distribution are impossible because the number of reported cases is too small to be of any statistical significance. There does not appear to be any particular frequency in any one age group as will be noted in table 1. It has not appeared before adolescence and only infrequently beyond the sixth decade. The oldest reported case was 71 years old (*8*). According to Trotter and Eden (*6*) there has been no correlation of the age distribution of circumscribed pretibial myxedema with that of thyrotoxic cases in general.

TABLE 1.—*Age and sex distribution in 67 cases*

Age (years)	Male	Female	Not recorded	Total
Under 20		1		1
20-29	4	4		8
30-39	5	11	1	17
40-49	6	13		19
50-59	5	6		11
Over 60	2	6		8
Not recorded	1	2		3
Total	23	43	1	67

Approximately twice as many cases have been reported in women as in men.

Practically all the cases in which race was mentioned were in Caucasians although its occurrence in two Negroes (*2*) (*9*), one Chinese (*10*), and one Dravidian (*11*) has been reported.

Bilateral circumscribed pretibial myxedema was found closely associated with exophthalmic goiter. Diffuse toxic goiter existed in all reported cases except four in which toxic nodular goiter was present (*10*) (*11*) (*12*) (*13*).

PATHOLOGY

Gross.—The changes consist typically of bilateral anterolateral pretibial cutaneous ovoid plaques about 7 cm. in diameter in the lower

or middle thirds of the pretibial areas. Considerable variation in size has been reported with the areas of myxedema even extending to the feet or around the ankles. The involved skin has the characteristic "pigskin" dimpling of cutaneous edema although it may be roughly nodular. The skin may be slightly inflamed but not characteristically so. Exudates from incised areas give a positive stain reaction for "mucin."

Microscopic.—Microscopically the characteristic pathologic feature is a splitting or dissection of the connective tissue fibers of the corium with interstitial spaces filled with mucin. No inflammatory changes are ever evident and the epidermis is normal.

The pathology of pretibial myxedema has been more fully discussed by Pillsbury and Stokes (*2*).

The time of onset or discovery of the pretibial lesions in relation to the thyroid disease does not permit any conclusions. In a number of cases the lesions have appeared in the course of recurrent or residual thyrotoxicosis following thyroid surgery. Many of the cases have had the onset of pretibial lesions in an interval of 1 or 2 years after the appearance of thyrotoxicosis or after thyroidectomy. In the majority of cases there is a wide variation in onset—from 1 to 2 weeks (*14*) to over 10 years (*13*). Table 2 gives the time of onset of pretibial lesions in regard to the course of the thyroid disease.

TABLE 2.—*Onset of bilateral pretibial myxedema in 77 cases*

Before the onset of thyrotoxicosis (*15*)	1
Before treatment for thyrotoxicosis	34
After thyroidectomy	40
After high-voltage roentgen treatment of thyroid	2

Clinically the most striking feature is the unvarying occurrence of pretibial mucin deposition in association with recurrent, residual, or controlled exophthalmic goiter. These features are so characteristic that a clinical diagnosis can be readily made if one considers this syndrome among the diagnostic possibilities. Lymphedema and scleroderma must be considered in the differential diagnosis.

The lesions are rather indolent in their course. They are said to regress and disappear spontaneously over a period of years (*2*) (*6*) (*7*) (*13*) (*14*) (*15*).

As one would expect in an entity whose cause is unknown, treatment has been generally ineffective. Excision of the lesions was tried in one case with presumably a good permanent result (*15*). Local thyroxin (*6*) (*16*), thyroid extract (*2*) (*6*), radiant heat (*17*), iodine (*2*), and local thyroid implantation (*18*) have all been tried without apparent effect on the course.

SUMMARY

1. Bilateral circumscribed pretibial myxedema is an uncommon and not very important clinical entity consisting of bilateral pretibial plaques of mucin deposits occurring in association with a thyrotoxic state, usually exophthalmic goiter. It usually appears in recurrent or residual thyrotoxicosis following surgery.

2. Age, sex, and race distribution and incidence cannot be positively stated because only 84 cases (a statistically insignificant number) have been reported in the literature.

3. The pathologic feature consists of localized cutaneous mucinous infiltration, microscopically identical with that of classical myxedema of hypothyroidism.

4. In typical cases the diagnosis is readily made clinically. The differential diagnosis includes lymphedema and scleroderma.

5. An additional typical case is reported.

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Syndrome of Circumoral Pigmentation Associated With Generalized Intestinal Polyposis

Report of a Case

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HUTCHINSON (*1*) in 1896 published a report of identical twins who both presented a peculiar pigmentation about the mouth, a fact which was then regarded as a dermatologic curiosity.

Weber (*2*) in 1919 recorded the death of one of these twins from intussusception. Although there was no post-mortem confirmation of intestinal polyposis, it seems likely that these twins suffered from the syndrome to be discussed.

Peutz (*3*) in 1921 described a singular family, several members of which showed a strongly suspected or proved generalized intestinal polyposis associated with pigmentation of the mouth, hands, and feet. Because three generations of this family had intestinal polyps and skin pigmentation a definite familial trend of the disease was apparent. Peutz was the first to report this syndrome.

Van Dijk and Oudendal (*4*) reported the cases of a brother and sister who underwent surgical exploration because of repeated episodes of severe colic; intussusception of the ileum secondary to small bowel adenomas was found. It is to be noted that both the brother and sister had pigmentation of the lips present from birth, similar to that noted in our case.

Foster (*5*) in 1944 published the cases of a father and daughter who suffered from single small bowel polyps complicated by intussusception; they also showed characteristic circumoral pigmentation. The father's brother who also had similar lip and facial pigmenta-

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tion was subject to attacks of abdominal pain and bloody stools; he was found to have an inoperable carcinoma of the stomach. This man's son also had attacks of abdominal pain as well as an unusual pigmentation of the oral mucous membrane and lips.

Touraine and Couder (*6*) (*7*) reported a case of a similar syndrome in 1945. They abstracted the literature and collected some 31 cases that exhibited the pigmentation of this syndrome. However, only in Peutz, and Touraine and Couder's cases were intestinal polyps demonstrated. A definite familial incidence seemed to be present in their cases since a majority occurred in several generations of family groups.

In addition to the cases of established small bowel polyposis occurring in persons who have circumoral pigmentation, there are a number of incomplete case histories in the literature in which polyps of the intestine were either not looked for or could not be found after the usual diagnostic methods—without laparotomy (*8*).

Judging by the pictures published in Hutchinson's article, the twins represented examples of a type of pigmentation observed by others and which we report here.

Jeghers (*8*) (*9*) is primarily responsible for calling attention to this hitherto unappreciated syndrome. In 1944 he briefly reviewed the literature and mentioned two proved cases. Since that time Jeghers, McKusick, and Katz (*9*) have personally studied 8 additional cases and have made an extensive analysis of the hereditary aspects of the syndrome. According to them, the pigmentation is usually noticed during infancy or childhood, is most distinct on and about the lower lip mucosa and on the buccal mucous membrane, and in addition, may be found on the upper lip, and more rarely on the skin about the mouth and on the fingers and toes. The pigment ranges in color from brown to almost black, and is apparently melanin. The salient factor is that the labial and buccal mucosal pigmentation *must* be present in order to diagnose the syndrome; digital and facial pigmentation are merely complementary if found. The pigmentation must not be confused with ephelides (ordinary freckles) which do not occur on the mucous membrane of the oral cavity. Jeghers calls the buccal mucosal pigmentation the sine qua non of the syndrome. Further analysis of the 10 proved cases of Jeghers et al. (*9*) indicates that large bowel polyposis alone is not present in this syndrome, but that small bowel polyposis (principally jejunal polyps) with or without large bowel or stomach involvement is necessary if there is to be association with the pigmentary pattern.

It is our intention in presenting this case to call attention to this distinctive syndrome, which, if recognized, will permit early and

complete diagnosis of similar cases and prevent needless delay in instituting therapy.

CASE REPORT

A 10-year-old white boy was admitted to the National Naval Medical Center, Bethesda, Md., on 2 August 1949. He had been seen previously (July 1949) at a naval dispensary, at which time a roentgenogram revealed a large polyp of the colon.

His illness had its clinical onset when the patient was between the ages of 9 and 12 months—he then had his first episode of subnormal temperature, pallor, listlessness, abdominal distress, and repeated vomiting. Medical advice was sought, but no therapy was instituted because the symptoms subsided in a few days. When the child was between 9 months and 6 years of age he suffered five or six similar episodes, each characterized by sudden onset. During this entire period he was a sick, underweight child with many feeding problems; in particular, the morning meal was vomited shortly after eating. Many physicians

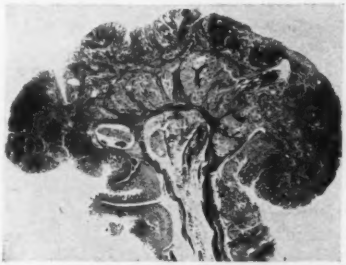

Figure 1.—Section of one polyp (2.8×1.7 cm.) removed from jejunum in 1944. (Low magnification.)

Figure 2.—Pigmentation on the lips and about the mouth.

were consulted and the general opinion was that the mother was not feeding the child correctly.

Past history.—In 1944, at the age of 6 years, another episode of what in retrospect appeared to be high intestinal obstruction occurred; the child was hospitalized for 15 days. Physical examination at that time revealed a soft, freely movable mass about the size of a large sausage, located just above and to the right of the umbilicus. Laboratory examination revealed: red blood cell count, 3,970,000; hemoglobin, 74 percent. The physician thought that the child's condition was caused by intussusception secondary to either congenital jejunal bands or a mesenteric cyst. An exploratory laparotomy was performed, and a double intussusception, two healed ulcer areas (one close to the ligament of Treitz, the other about 12 inches distant), and two solid obstructing polyps were found in the jejunum. A segmental resection and an end-to-end anastomosis was performed and the patient was discharged from the hospital in excellent condition. Sections of one large jejunal polyp 2.8 × 1.7 cm. (fig. 1) obtained at the time of this operation were reported as a benign jejunal polyp. Since the operation in 1944 there has been no recurrence of intestinal obstruction.

One year later, several polyps protruding from the boy's anus were excised. The patient's family was advised that he should have yearly barium enema

Figure 3.—Barium enema contrast study showing the presence of a large polyp in the descending colon.

studies and a proctoscopic examination. When he was between the ages of 7 and 8 years, five or six new rectal polyps were discovered and excised. Again, at the age of 8, another rectal polyp was fulgurated. The patient had no more difficulty until July 1949 when a large polyp of the colon above the rectosigmoid level was revealed by roentgenogram. This necessitated hospitalization and brought the case to our attention. It should be emphasized that the original diagnosis of small bowel polyposis was not made for a period of 5 years after the onset of symptoms, even though the characteristic pigmentation was present from birth. This pigmentation had been noted by a number of physicians who, however, were unaware of its significance.

The family history was entirely negative for gastrointestinal symptoms except for "hemorrhoids" in three persons of the paternal line.

On admission to this hospital the patient appeared to be normal, well-nourished, and well-developed. There was slight inflammation of the pharynx and a postnasal drip. The mucous membrane of the lower lip was diffusely mottled with dark grayish black pigment deposited in patches of varying size (fig. 2). These lesions were not elevated. On the skin about the lips there were a lesser number of similar lesions, some slightly elevated. In addition a few pigmented areas were present on the upper lip and some were also present on the oral mucosa. The temperature was 99° F.; the blood pressure, 110/70; and the pulse, 82.

Laboratory examination showed: red blood cell count, 4,100,000; hemoglobin, 11 gm.; white blood cell count, 5,500.

On 8 August 1949, a barium enema contrast study showed a polyp, measuring 17×20 mm., in the lower descending colon (fig. 3).

On 11 August 1949 a laparotomy was done and a large polyp was excised through an incision in the sigmoid colon. Pathologic examination revealed a benign pedunculated adenomatous polyp measuring 1.5×2.0 cm. (fig. 4).

The postoperative course was uneventful, and the boy was discharged on 20 August 1949.

Figure 4.—Section of polyp removed in 1949. (Low magnification.)

SUMMARY AND CONCLUSIONS

A case of small and large bowel polyposis associated with a characteristic pattern of circumoral pigmentation is presented. This case is probably a sporadic instance of a syndrome which is usually clearly hereditary and transmitted as a simple mendelian dominant.

This syndrome is not generally appreciated, and when pigmentation of the type described is seen, small and large bowel polyps should be diligently searched for by roentgen studies of the gastrointestinal tract and by sigmoidoscopic examination.

When symptoms of abdominal colic or intestinal obstruction occur in a patient with this distinctive type of circumoral pigmentation, generalized intestinal polyposis should be suspected.

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Cutaneous Diphtheria

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FREDERICK G. NOVY, *M. D.*

CUTANEOUS diphtheria is rare in this country. Thorough reviews of the subject are found in reports by Army medical officers from the South Pacific (*1*) and the India-Burma (*2*) areas. Wound diphtheria is not to be confused with cutaneous diphtheria. Of the latter, there are two types, and the more common is the ulcerative lesion of the skin arising from secondary infection by *Corynebacterium diphtheriae* of preexisting skin lesions such as insect bites, burns, and abrasions. The other form is an eczematous type resulting from diphtheritic infection of a preexistent eczematous lesion. Presumably an eczematous reaction to a diphtheritic infection could occur without the presence of a preexistent eczematous process. Any eczematous process in a person believed to have been exposed to diphtheria should be examined for the presence of *C. diphtheriae*. Epidemic cutaneous diphtheria ordinarily occurs only in tropical or desert climates where sporadic cases occur frequently. They are infrequent in temperate climates.

CASE REPORT

A 25-year-old soldier was admitted to this hospital on 30 December 1947. His present illness began about 2 months previously while he was stationed near Tampa, Fla. He had not been out of Florida in several months preceding the onset of the illness. He first noticed numerous small papules on the dorsum of his right foot. As these lesions coalesced, the central area ulcerated and extended peripherally until an ulcer about 2.5 cm. in diameter was formed. Within the next few days, the patient noticed a similar small ulcer in the right popliteal space and another in the flexural crease of the base of the fifth right toe. Later, he noticed additional single lesions on the dorsum of the right foot, on the dorsum of the right fifth toe, in the left popliteal area, and on the left buttock. Following a 5-week treatment with various ointments without improvement, he was transferred to a station in California where he was hospitalized in a station hospital on 7 December and treated with bed rest, boric-acid compresses, heat, and a total of 1,550,000 units of penicillin given intramuscularly. Penicillin was

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discontinued because of the occurrence of a generalized urticaria that was thought to be due to a reaction to the drug. At this time, his skin lesions were described as oval, shallow ulcers with dirty bases, and a punched-out appearance. One lesion had a firm, adherent, black central slough. Smears for fungi, yeasts, and acid-fast bacilli were negative, but gram-positive cocci and small spore-forming rods were seen. Under the treatment described the lesions became clean, but no healing occurred, and the patient was transferred to this hospital.

Figure 1.—Before treatment.

On admission here, the ulcer on the dorsum of the right foot (fig. 1) was 2.5 cm. in diameter and had a black, adherent, leathery central slough that did not cover the entire area of the ulcer. Surrounding the slough was a dirty, purulent exudate. The edges of the ulcer were slightly raised, rolled, and violaceous. The inflammatory erythema extended several millimeters beyond the ulcer margin. The ulcer on the fifth toe had extended to involve two-thirds of the toe's circumference. It was covered with a dirty, gray-yellow exudate, and had a punched-out appearance. The other lesions were similar in appearance. None of these had a central slough. At this time the lesions were extremely painful and tender to touch, and cleansing and dressing them caused great discomfort. The patient assumed awkward positions in bed to avoid even the slightest pressure on the lesions.

The clinical impression of cutaneous diptheria prompted the taking of cultures. These were positive for *C. diphtheriae*. By animal inoculation, the strain was found to be mildly virulent. Nose and throat cultures were negative for *C. diphtheriae* throughout the patient's hospitalization. After the laboratory confirmation of the diagnosis of cutaneous diphtheria, the patient received 50,000 units of diphtheria antitoxin. Within 1 hour after its administration, the local pain of the lesions was relieved. After 24 hours, the bases of the ulcers were more clean, the edema decreased, and the surrounding skin had a more healthy appearance. The patient received an additional 30,000 units of antitoxin 3 days after the first dose. Local treatment consisted of peroxide cleansings and boric-acid solution and saline compresses. Penicillin, which has been described as being the most effective of local measures (*3*) was not used because of the previous urticarial reaction.

Figure 2.—After treatment.

Following this treatment, epithelialization of the margins with advancement centripetally occurred, leaving a thin, smooth, pale, sharply demarcated scar (fig. 2). There was no evidence of *C. diphtheriae* in the scars up to 1 month after healing. A moderately severe polyneuritis occurred 3 months after the onset of the cutaneous ulcers. This was manifested by paresthesia of the fingers and toes, fine digital tremors, general weakness, muscular fibrillary twitchings, hyperesthesia, hypesthesia, decreased vibratory sense, and a spinal fluid protein of 69 mg. per 100 cc. A high-caloric, high-protein, high-carbohydrate diet with supplemental vitamin therapy was prescribed. His response was slow, but persistent. There was no known history of exposure to cutaneous or nasopharyngeal diphtheria.

DISCUSSION

Multiple lesions, as seen in our patient, are reported in 75 percent of the cases of cutaneous diphtheria. Unhealed, indolent ulcers that are severely painful soon after onset but show hypesthesia and anesthesia of the base, margin, and surrounding periphery of the ulcer 3 to 5 weeks after the onset, suggest the diagnosis of cutaneous diphtheria (*2*). In this case, the presence of severe pain in the ulcers about 8 weeks after the onset conflicts with this diagnostic criterion. The diphtheritic infection in this patient may not have occurred at the time of onset of the ulcerations of the skin, but may have been superimposed several weeks later. If this were true, the nature of the original ulcerations would remain obscure. Myocarditis, proportionate to the severity of the diphtheritic infection and occasionally fatal, occurs 4 to 7 weeks after the onset in a small percent of cases. Our patient showed no evidence of myocardial involvement.

SUMMARY

A case of cutaneous diphtheria that occurred within the United States, and conformed to the current descriptions of cutaneous diphtheria was complicated by a polyneuritis. The patient responded favorably to local cleansing measures, bed rest, and diphtheria antitoxin. Penicillin was without effect. Indolent ulcers necessitate consideration of the diagnosis of cutaneous diphtheria, even in nontropical and nondesert climates.

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Glanders

RALPH W. MENDELSON, *Lieutenant Colonel U. S. A. F. (MC)*

GLANDERS, an acute infectious disease of equines caused by *Malleomyces mallei*, is characterized by ulcerating granulomatous lesions of the skin, subcutaneous tissues, and mucous membranes. The acute cases may become chronic and the chronic cases exhibit acute exacerbations.

In humans it is frequently fatal and often difficult to diagnose unless one is cognizant of the disease when dealing with ulcerating, granulomatous lesions of the skin and/or mucous membranes. The protean manifestations in both the acute and chronic stages may suggest a number of clinical conditions and valuable time may be lost in protecting contacts if a patient with this condition is undiagnosed and thus permitted to spread the infection.

A positive diagnosis cannot be made on clinical findings alone. A history of contact with horses, mules, or donkeys is highly suggestive in a patient exhibiting an ulcerative, granulomatous lesion, particularly of the nose. Syphilis, tuberculosis, epithelioma, and/or a variety of other diseases including granuloma inguinale, lymphogranuloma inguinale, and mycotic lesions must be ruled out.

The following cases were collected by the author and portray the chronic type of lesion. Each patient gave a history of contact with either horses or donkeys. The diagnoses were confirmed bacteriologically. Because of the virulence of the organism it is not advisable to work with cultures except under the most meticulous bacteriologic technique.

CASE REPORTS

Case 1.—A 36-year-old white woman with lesions as shown in figure 1 presented herself for treatment. The past history was irrelevant except for the fact that she had been living on a farm and had been in daily contact with two horses that had died of an unknown disease. She had been treated for a variety of conditions without results. Except for the presenting condition, physical examination was negative. Smears from the nasal discharge and from the ulcers revealed an infection with a gram-negative, slightly curved rod that proved to be

Figure 1.

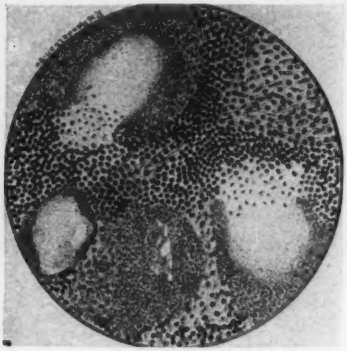

Figure 2.

Mallcomyces mallei. The patient's serum agglutinated *M. mallei* in high dilutions. Biopsy of a section of tissue (fig. 2) showed granulomatous lesion—masses of epithelioid cells with central necrosis, and abundant leukocytic infiltration. Giant cells were not observed.

Case 2.—A Mexican youth, aged 15, presented himself for treatment because of the loss of the sight in his left eye, a severe infection in his right eye, a profuse mucopurulent nasal discharge, and extensive ulceration of his lips and nose (fig. 3). The past history was negative except for the fact that he lived on a ranch and had been in daily contact with a horse that died of an unknown disease. The infection first manifested itself in the patient's left eye, followed by a mucopurulent nasal discharge. Ulceration of the nose and lip followed

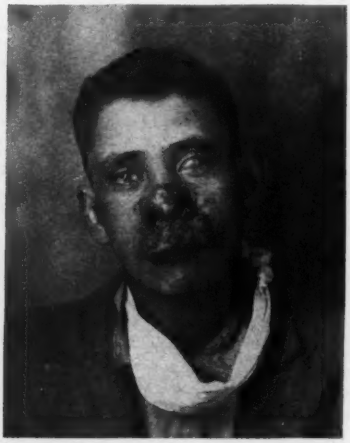

Figure 3.—Case 2. Appearance of patient on admission.

Figure 4.—Case 2. Improvement after being treated with vaccine.

and this in turn was followed by irritation of the throat and some difficulty in swallowing. The right eye became infected about 6 months prior to the present examination. At no time did the patient have severe constitutional symptoms. Examination revealed moderate corneal ulceration of the right eye with extensive conjunctival inflammatory reaction and moderate discharge. The left eye presented the same condition, but to a much more extensive degree with profuse discharge and complete loss of vision. The nasal passages were blocked with encrusted discharge; the throat lesions were subacute; the palate and tonsils were not involved.

Bacteriologic examination of secretions from the eye, nose, and skin lesions revealed a mixed infection of *Staphylococcus aureus*, a diplococcus, and many gram-negative, slightly curved rods with irregular staining properties that proved to be *M. mallei*. The patient's serum agglutinated *M. mallei* in high dilutions. He was treated with vaccine and made satisfactory progress (fig. 4).

Figure 5.

Figure 6.

Case 3.—The patient, a German prisoner of war, stated that he had been blown up by a land mine. His injuries at the time were not serious except for severe contusions and abrasions to the chin. He had worked with donkeys, but did not recall that any of the animals were sick or that any of them had died of disease. The fact that he was in daily contact with these animals is of primary importance in the epidemiological history.

Complete physical examination was negative except for an ulcerating, granulomatous lesion of the chin as shown in figure 5. The condition had been present for several months. Treatment had been symptomatic and without results. Bacteriologic examination revealed typical *M. mallei*. A foreign culture could not be obtained at the time for agglutination with the patient's serum.

Case 4.—A sheep herder had been treating himself for a number of years with a variety of ointments and home remedies. He owned a donkey at one time, but the animal died shortly before the patient became ill. His condition first manifested itself by a mucopurulent nasal discharge followed by ulcerations of the nose

and lips with the formation of extensive scar tissue and deformity. Nasal obstruction was complete (fig. 6). There was considerable bilateral adenopathy, but no glandular necrosis. An organism that proved to be *M. mallei* was obtained from the nasal ulcerations; this patient's serum also agglutinated *M. mallei* in very high dilutions.

DISCUSSION

The past history in all of these cases reveals that each patient had been in close daily contact with either horses or donkeys and that in every case except one, the animals had died of some unknown disease.

Clinically the lesions may be confused with a variety of conditions. The author has observed, in the tropics, early gangosa that simulated glanders.

The prognosis is not good; the author knows of no specific treatment. Vaccine treatment in case 2 appeared to be of value but one should be cautious in pronouncing a cure as latency is characteristic of the disease.

The nasal passages appear to be the portal of entry for the infection although in one of our cases the eye was apparently the site of the primary lesion.

Foot-and-Mouth Disease in Mexico

THOMAS G. MURNANE, *First Lieutenant, VC, U. S. A.*[1]

THE most serious threat to our cattle today is foot-and-mouth disease, now prevalent in Mexico. Our animal population has suffered from 10 previous outbreaks, the first in 1870 and the latest in 1932. Aside from the present outbreak in Mexico, the cattlemen in Europe, Asia, Japan, Africa, and South and Central America have contended with this malady for many years.

In Mexico the mortality from this disease has been low. In outbreaks in other countries, the animal populations have been more seriously affected. Lesions are usually confined to the mouth, hoof, and udder. After an incubation period of from 18 hours to 1 week, vesicles, that later rupture, appear in the mouth, in the cleft of the hoof, or on the udder. If the tongue is involved there is usually complete loss of the lingual epithelium. However, the stratum germinativum is not affected, perhaps accounting for the rapid recovery in cases without secondary involvement. In many cases infection of the hoofs has been followed by a secondary invasion with *Actinomyces necrophorus*, producing serious lameness.

An outbreak of the disease results in severe economic losses. Milk production is seriously affected in all types of dairy cattle. This disease is highly infective and spreads to entire herds and over large areas. There is no other known disease of animals whose infectivity is greater. An example is the milk shed of Mexico City where at least 50 percent of all dairies were infected. Beef cattle suffer great loss of weight, and may abort. All cloven-hoofed animals—cattle, sheep, swine, and goats—are susceptible. Horses are not affected and there have been no cases in wildlife reported in Mexico.

There are at least three types of foot-and-mouth disease virus—A and O (from the villages of Ardennes and Oise in France where these types were originally isolated) and C. Until recently only type A

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virus had been demonstrated in Mexico. In the fall of 1949 type O was isolated in an outbreak about 18 miles north of Mexico City. In this instance all the infected animals were slaughtered and the area was quarantined. Whether the isolation of this strain will present a serious problem is not yet known. Animals that have acquired an immunity to type A, through a natural infection or vaccination, are susceptible to type O.

With knowledge gained from our past experiences, a commission was formed with representatives of the Mexican Government for the eradication of foot-and-mouth disease from Mexico, and to eliminate this serious threat to our large and valuable animal population. The plan being employed by the American and Mexican Commission in the extermination of this disease includes inspection, quarantine, slaughter when necessary, disinfection, and vaccination in the order of importance. In order that this plan may be operated under close and constant supervision, the infected zone has been divided into nine districts, and each district is further divided into subdistricts and areas. Each is under the supervision and control of American and Mexican veterinarians. The area is the smallest operational unit; to each unit, veterinary supervisors, livestock inspectors, vaccinators, and disinfectors are assigned.

The original all-out slaughter program was abandoned in the latter part of 1947 because of the severe economic strain on the country and the resulting hostility. In its place the previously mentioned program was adopted. In spite of certain modifications, the program is still opposed in many sections and inhabitants resist the inspection or vaccination of their cattle. In consequence, numerous Mexican military personnel are being employed to aid in enforcing the program.

VACCINATION PROGRAM

The vaccine used in Mexico is produced by laboratories in Mexico City. It is applied intradermally in doses of from 1 to 2 cc., depending on the size of the animal. Its production is costly since only 200 doses of vaccine may be produced from the tongue of an inoculated animal. The average output is about 1 million doses a month. A method of cultivating foot-and-mouth disease virus in tissue explantations, as developed by Frenkel, has been in use at the State Institute for Veterinary Research, Amsterdam, Holland. Originally the virus was grown in surviving embryonic bovine, ovine, and porcine skin tissue. Now a method has been developed for cultivating the virus in explanted epithelial tongue tissue. Possibly, by this method, more economic production of virus for vaccine preparations may be accomplished.

Natural infection does not confer a permanent immunity and the vaccine that is being used, although reportedly the best available today, produces an immunity that lasts only about 4 months, necessitating a series of vaccinations of about 13 million animals in the infected zone. Possibly with the isolation of the type O virus a bivalent vaccine may be produced. To date the first vaccination has been completed, the second is in progress, and the third was started recently. The vaccination has been conducted from the northern and southern boundaries of the infected zone and directed toward the center of the zone. Because of the tremendous number of animals involved, it has been necessary to employ laymen as vaccinators. These men are trained in the procedure and technique of vaccination and their work is observed by inspectors—one inspector for each five vaccinators—as well as by the veterinary supervisors.

The most important phase of the program is the inspection and observation of every bovine, ovine, caprine, and porcine animal within the infected zone. Not only are the results of the vaccination observed, but all animals are observed periodically for symptoms or signs of the disease. At present a number of inspectors are assigned to each area supervisor for this work. With sufficient personnel monthly inspections can be conducted within each zone and with such constant vigilance all suspicious cases can be immediately reported to the veterinarian for his provisional diagnosis and subsequent action. Inspection and quarantine stations are maintained at all exits from the infected zone. The movement of cattle from the infected to the uninfected zone is absolutely forbidden. All vehicles are disinfected, and goods which might carry the virus are not permitted to be removed. A strict quarantine is observed in all infected areas and the premises are thoroughly disinfected following the slaughter of infected animals.

Although there has been no infection reported for the past several months, monthly inspections of the animals within the infected zone have reached only about 60 percent of the estimated population. In the remaining 40 percent whose status is unknown, it cannot be said that infection is absent. If we accept the evidence that under favorable conditions the virus remains viable on the ground for 8 months, and that carriers may harbor the virus within the structure of the hoof or in the blood and urine for an equal period, then it is reasonable to assume that until monthly inspections of the entire animal population within the infected zone are accomplished and no infection observed for a period of 1 year, can the fight against hoof-and-mouth disease be considered to be won.

Bony Lesions Occurring During The Early Stages of Syphilis

Report of a Case

JOHN H. COX, *Commander (MC) U. S. N.*[1]

EVERY physician is familiar with the fact that lesions of the skeletal system, especially destructive osseous lesions, occur during the tertiary stage of syphilis. That this should be true is a little difficult to understand, since it is a well known fact that very early in the course of the disease vast numbers of *Treponema pallidum* are widely distributed throughout the entire body, and every tissue in the body harbors the organism (*1*) (*2*).

In 1942, Reynolds and Wasserman (*2*) reviewed the literature and found that 15 cases had been reported. In addition to these, they reported 15 additional cases taken from 10,000 cases which had been observed in the syphilis division of the medical clinic and on the wards of the Johns Hopkins Hospital over a 22-year period (1918 to 1940). Review of the available literature today reveals that theirs is probably the most extensive study of this particular manifestation of the disease which has been made. As early as 1916, Wile and Senear (*3*), in a study of the involvement of the bones and joints in early syphilis, reported that 60 (36 percent) out of 165 patients with signs of either primary or secondary syphilis also showed signs of bone or joint involvement. Their rather extensive study was completed without the aid of roentgenologic examinations, except in the suspicious cases, and it is entirely possible that a higher percentage would have been discovered had roentgenograms of the bony skeleton been available in all cases. Bloom (*4*), in June 1934, reported a case of destructive osteitis and facial paralysis in secondary syphilis. His patient apparently had no symptoms referable to the skeletal system until after antiluetic therapy was instituted. Following two injections of bis-

[1] U. S. Naval Hospital, Aiea Heights, T. H.

muth and one injection of neoarsphenamine the patient had pain in the left acromioclavicular articulation over which appeared a tender swelling, and pain on motion of the arm. Roentgenograms showed a destructive lesion in the outer end of the left clavicle. After further antiluetic treatment, healing was demonstrated. Squires and Weiner (*5*), in 1939, reported a case of osteitis of the skull in early syphilis. They stressed that bone involvement would be discovered more often if roentgenograms were made when patients with early syphilis complained of headache. Newman and Saunders (*6*), in 1938, reported multiple areas of destruction of the inner and outer tables of the skull in a case of secondary syphilis. They stated that osseous lesions of early congenital syphilis were analogous to those of early acquired syphilis. Every student of syphilology is acquainted with the fact that skeletal involvement is fairly common as a relatively early sign in congenital syphilis. Mandelbaum and Saperstein (*7*), in 1936, reported a case of acute gummatous osteomyelitis of the skull and the sternum 8 weeks after blood transfusion. Pian and Frazier (*8*) reported a similar case in 1940. Thompson, Leedham, and Hailey (*10*), in 1949, reported two cases of osteomyelitis of the skull occurring during early syphilis, each one occurring during the secondary stage of the disease. They felt that trauma might have played a part in determining the location and the subsequent destructive course of the bone lesions. One of their cases also showed a periostitis of each tibia, and the other showed a similar involvement of the right humerus. Interestingly enough, one of these patients was admitted to the hospital for a fracture of the second cervical vertebra, but never showed signs of luetic involvement in this location. The case reported in this article did not give a history of trauma. Likewise, the majority of cases reported in the literature to date have failed to give a history of trauma.

It seems to be almost universally agreed that more cases would be discovered if careful physical examination and roentgenologic examination of the skeletal system were done in all cases of early syphilis. Patients frequently complain of headache during the early weeks of the disease; however, roentgenographic studies are seldom done, unless the patient complains of severe pain. Then, too, because of the dearth of literature regarding this condition it is probable that few physicians are well acquainted with the fact that organic bone lesions, periostitis, arthralgia, arthritis, osteoperiostitis, or osteomyelitis of various parts of the skeletal system can occur during the early weeks or months following the introduction of the causal organism into the body. According to Pancost, Pendergass, and Schaeffer (*11*), luetic invasion of the calvaria is generally limited to the anterior and lateral portions of the skull, extension being halted by the lambdoid suture.

Destructive gummatous lesions of the skull, the central portion of the face, the tibia, the sternoclavicular region, and the shoulder girdle, occurring years after the primary lesion, are well known to everyone.

CLINICAL FINDINGS AND DIAGNOSIS

The diagnosis of destructive bone lesions in early syphilis depends upon an accurately taken history, careful physical examination, and skillfully interpreted roentgenograms. The serologic test is practically always positive. The most frequent lesion seen is a proliferative periostitis of the tibia. Other types of involvement are ostalgia, osteitis, osteoperiostitis and osteomyelitis. Arthralgia and arthritis may accompany the process. The bones most frequently involved in the destructive type of lesions are those of the skull. Pancost, Pendergass, and Schaeffer (*11*) make the startling statement that few individuals infected with syphilis escape some skull involvement, but, due to lack of symptoms referable to the head, the skull is not often studied. However, any bone in the body might be involved in one of the above-named processes. The most frequent symptoms are pain and swelling at the site of involvement. According to some observers, the pain is worse at night, but, according to others nocturnal pain has been unduly overstressed. Some observers state that for some unknown reason the pain seems to be worse while the patient is in the reclining position. This is questionable. The fact that the patient complains more of pain at night while in the reclining position is possibly due to the fact that his attention is more likely to be attracted to his condition when his mind is relieved of the daily distractions. The patient reported in this article did state that his pain was worse at night. In discussing syphilitic periostitis, Stokes, Beerman, and Ingraham (*9*) state:

> Early syphilitic periostitis, clinically, is a sharply localized process seldom covering more than a few square centimeters and presenting as a somewhat doughy elevation on the bone, noninflammatory, without any sign of fluctuation. * * * Its most distinctive feature is the highly localized point of exquisite tenderness which can be found by searching the entire surface of the tumefaction with the fingertip.

Any sign or symptom of secondary syphilis might accompany these osseous lesions. Bone lesions may occur anywhere from 6 weeks after the primary lesion to 14 months after the appearance of the secondary lesions (*2*). Several cases have been reported in which rather marked systemic symptoms occurred, including chills and fever, malaise, anemia, weakness, and loss of weight.

ROENTGENOLOGY

According to Stokes, Beerman, and Ingraham (*9*), the importance of skilled interpretation of the roentgenogram is second only to rou-

tine serologic tests for syphilis in establishing the diagnosis of skeletal syphilis. It is agreed that syphilis is primarily a constructive or osteoplastic process. According to Stokes et al. (*9*), preponderantly constructive bone lesions are usually due to osteomyelitis or syphilis, and preponderantly destructive lesions are usually tuberculous or malignant. They also state:

> The chief exception to the constructive or productive rule in syphilis is in the case of the cranial bones, in which the ultimate destructive process, without reconstruction, leaves the diagnosis suspended between syphilis and malignancy. Since primary malignancy of the cranial bones is uncommon, it follows that a destructive process in the cranial bones is, in the absence of primary malignant focus elsewhere, almost surely of syphilitic origin, especially in a patient of precancerous age.

TREATMENT

The response to treatment is usually satisfactory and the reversal of the serologic test for syphilis is brought about. According to Reynolds and Wasserman (*2*), two of their cases apparently were extremely resistant to treatment, but eventually responded after extensive and heroic treatment, including fever therapy and massive arsenical treatment. The Herxheimer phenomenon may occur.

PATHOLOGY

Is this particular lesion to be considered a gumma? The answer has to be yes and no. If one adheres to the definition of a gumma, namely, "a soft gummy tumor occurring in tertiary syphilis and made up of tissue resembling granulation tissue," then the answer is "No." However, histologically this lesion is one of bone destruction with round cell infiltration most marked about the blood vessels. In one of the cases reported by Reynolds and Wasserman, a biopsy was done, and a more or less characteristic histologic picture of gumma was noted.

CASE REPORT

A well-developed, well-nourished 21-year-old white man was first seen on 20 April 1948 complaining of pain and left-sided headache of about 4 weeks' duration. Coincident with the onset of pain, he became aware of a small, tender swelling over the left frontal region. Roentgenograms of the skull then showed an area of bony destruction, measuring 2 cm. in diameter, located in the left frontal bone just anterior to the frontoparietal suture. A provisional diagnosis of neoplasm of the skull was made and the patient was transferred to a hospital ship on the same day. There physical examination showed: a tender swelling, measuring approximately 4×2.5 cm., over the left frontal region and slightly elevated above the surface of the skull; a faint macular rash over the upper anterior thorax; and enlarged, nontender, discrete lymph nodes in the posterior cervical, preauricular, postauricular, and axillary groups.

Physical examination in hospital.—The patient was later transferred to a naval hospital where the history and physical findings were essentially as given

above except that no rash was noted over the upper anterior thorax as previously described.

Past history.—According to the record and his story, in December 1947 the patient was treated for gonorrhea with 400,000 units of penicillin; his urethral discharge did not disappear entirely until 10 to 12 days after penicillin therapy had been completed. The patient stated that a blood Kahn test, 3 months after discontinuance of penicillin therapy for gonorrhea, was reported as negative.

Laboratory examination.—All laboratory studies, including tests for Bence-Jones protein, blood calcium, serum phosphorus, and serum phosphatase, and the tuberculin test were negative. Blood Kahn test, 3+. Spinal fluid examina-

Figure 1.—Anteroposterior appearance of skull before treatment (5 May 1948).

Figure 2.—Lateral appearance of skull before treatment (5 May 1948).

tion, normal. Complete urologic study and eyeground examination revealed no abnormalities.

Stereoscopic and roentgenographic examinations.—Stereoscopic examination of the skull showed an area of bone destruction measuring approximately 3 cm. in diameter and involving both the inner and outer tables of the left frontal bone just anterior to the left frontoparietal suture. Within the center of this rarefied area there was a zone of normal bone density measuring about 1 cm. in diameter (figs. 1 and 2). Roentgenograms of other bones and of the chest were negative.

Differential diagnosis.—The following conditions were considered in the differential diagnosis: Primary bone neoplasm; metastatic neoplasm, with the primary focus in some other part of the body; hemangio-endothelioma; eosinophilic granuloma; osteomyelitis, pyogenic; leutic osteomyelitis; Hand-Schüller-Christian disease; xanthomatosis; osteitis fibrosa cystica; Hodgkin's disease; and leukemic infiltration.

Darkfield examination.—It was considered that if the generalized adenopathy was luetic in origin, spirochaetes would more than likely be found in the lymph nodes. A lymph node was excised and a scraping, taken from the cut surface, on darkfield examination showed numerous spirochaetes and the typical morphology and motility of *Treponema pallidum* were observed. The destructive bone process, therefore, was considered to be luetic in origin, occurring in the early stages of syphilis.

Treatment.—Antiluetic therapy was instituted and the patient received the following treatment: From 15 May 1948 to 30 May 1949, penicillin, 10,000,000 units. From 15 May 1948 to 15 January 1949, mapharsen, 25 injections (total of 1.44 gm.), and bismuth subsalicylate in oil, 25 injections (a total of 3.25 gm.) were given. Simultaneously potassium iodide, 30 drops 3 times a day, was given and continued for 3 months. Additional arsenical and heavy metal therapy were given because (*a*) skeletal syphilis is generally considered to be one of the more difficult forms of the disease to eradicate, and (*b*) because it would not have been possible to adequately follow the case to determine whether a cure would have been accomplished with penicillin alone.

Figure 3.—Anteroposterior appearance of skull on 7 January 1949 after completion of antiluetic treatment.

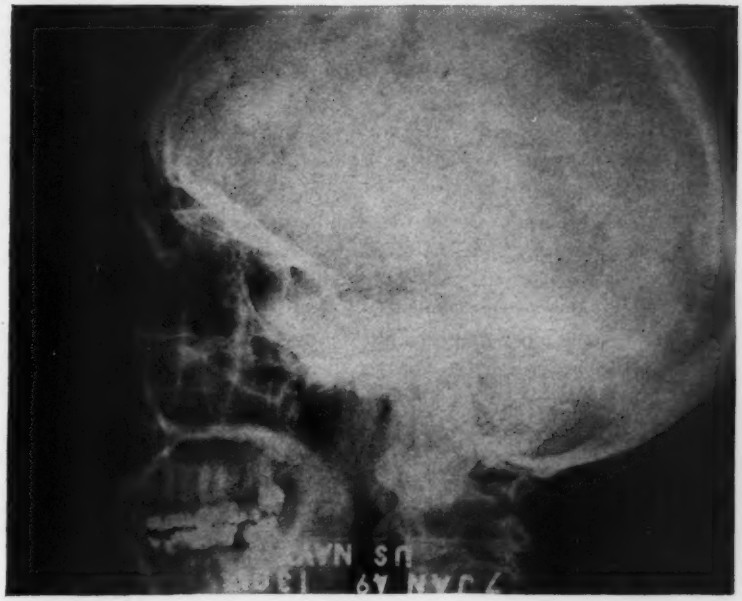

Figure 4.—Lateral appearance of skull on 7 January 1949 after completion of antiluetic treatment.

Healing of the destructive process occurred approximately 8 months after beginning antiluetic therapy (figs. 3 and 4). The blood Kahn test was reported negative December 1948, 7 months after antiluetic therapy was started.

DISCUSSION

The patient's blood Kahn test was negative when he entered the service in September 1945. In December 1947, he had gonorrhea which was treated with 400,000 units of penicillin—adequate therapy for the majority of cases of gonorrhea, but certainly inadequate for early syphilis although perhaps enough penicillin was given to mask the development of full-blown secondary syphilis. Since his urethral discharge did not clear up for 10 to 12 days following therapy for gonorrhea, that probably was indicative of the presence of an intraurethral chancre at that time. The macular rash over the upper anterior thorax before his admission to the hospital could easily have been an abortive secondary eruption.

SUMMARY AND CONCLUSIONS

A case of destructive syphilitic osteomyelitis of the skull occurring during the early stages of the disease is reported. A review of the literature shows that surprisingly few cases of this particular mani-

festation of the disease have been reported. Experts in the field have stated that more cases would probably be discovered if more careful physical examinations and roentgenologic studies were done during the early stages of the disease.

It has been suggested that bone involvement in early acquired syphilis is analogous to skeletal lesions commonly observed in the congenital form of the disease.

A very useful and practical method of making the diagnosis of syphilis is by lymph node aspiration or by lymph node excision and darkfield examination of the lymph node juice. This is especially true when skin or mucous membrane lesions are absent.

A plea is once more made to physicians who are charged with the responsibility of treating gonorrhea with penicillin to adequately follow such patients for a sufficient time, at frequent intervals, by physical examination and blood tests to rule out the possibility of a simultaneous luetic infection. Monthly physical examination and blood tests for at least 6 months after the completion of penicillin treatment of gonorrhea is considered necessary.

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Fractures of the Mandibular Condyle

Report of Eight Cases

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FRACTURES of the mandibular condyle are not so common as those which occur in other parts of the mandible. However, they are not so rare as was believed at one time. Their greater frequency may be attributed, at least in part, to the increased prevalence of automobile and industrial accidents. Furthermore, the better roentgenographic equipment and techniques now used show these fractures more clearly. Clinical statistics show that about 8 percent of mandibular fractures occur at the condyle.

ANATOMIC CONSIDERATION

The temporomandibular joint is complicated in that it is made up of the roller-shaped head of the condyle, the interarticular disk, known as the meniscus, and the mandibular or glenoid fossa. The fossa is bounded anteriorly by the articular eminence, and posteriorly by the postglenoid tubercle. The wall of the temporomandibular joint is a loose, thin capsule which surrounds the cartilaginous articular portion of the mandibular fossa and articular tubercle, and inserts in the area of the upper condylar neck. The joint cavity is divided into two chambers by a specialized disk of fibrocartilage which unites peripherally with the capsule and anteriorly with the insertion of the external pterygoid muscle. Laterally, the joint capsule is reinforced by the heavy bands of the temporomandibular ligament extending posteriorly and interiorly from the zygomatic arch to the lateral and posterior surface of the condylar neck.

The slinglike action of this ligament is important in normal joint function. Medially, the capsule is thin and not well-supported. Rupture at this site with medial dislocation of the condylar head is frequently seen in fracture of the condyle. The stylomandibular and

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sphenomandibular ligaments are of less importance; they aid in maintaining the mandible in place when a fracture occurs. Overriding of the fragments frequently follows condylar fractures. This condition results from the powerful upward contraction of the masseter, internal pterygoid, and temporal muscles. The external pterygoid muscle plays an important role in the displacement that occurs in condylar fractures. This muscle has its insertion in the neck of the condyle and because of its anterior pull tends to displace condylar fractures anteriorly. Some of the superficial structures in proximity to the condylar process are the parotid gland, auriculotemporal nerve, superficial temporal vessels, and branches of the facial nerve. The internal maxillary artery and pterygoid venous plexus are important structures deep to the condyle.

CLASSIFICATION

Condylar fractures have been classified by Thoma (*1*) as follows:

1. Fractures without displacement.
2. Fractures with displacement.
3. Fractures with overriding of the fragments.
4. Fracture dislocations (medial or lateral).
   - *a.* Intracapsular fracture dislocations (subluxation).
   - *b.* Complete fracture dislocation.
   - *c.* Fracture dislocation with complete dislodgment of the condyle.
   - *d.* Dislocation of part of the head of the condyle.
5. Fracture dislocation in forward direction.
6. Fracture dislocations with displacement of the meniscus.
7. Comminuted condylar fractures.
8. Old condylar fractures with deformity.

ETIOLOGY

The cause is direct or indirect external violence. The fracture usually occurs as a result of a blow on the chin. If the blow is on the side of the chin, the opposite condyle is usually involved. In bilateral fractures, the blow is often on the point of the chin.

CLINICAL FINDINGS AND DIAGNOSIS

The clinical signs of fracture of the mandibular condyle may be scarcely perceptible and symptoms may be negligible or absent. Frequently the roentgenogram gives the first evidence of a condylar fracture. Varying combinations of signs and symptoms may be present, and there is no correlation between the extent of fragment displacement and the magnitude of clinical deformity. In spite of the displacement seen in roentgenograms, there may be no occlusal im-

balance or functional disturbance. Fractures with minimal displacement are usually unaccompanied by great deformity or functional disturbance. On palpation of the area in front of the ear, an absence of normal excursion of the condylar head will be found on the side of the fracture. Palpation of this area may reveal crepitus. If there is no associated edema, gross displacement of the condylar head may be disclosed by palpation. Pain may be present in front of the ear with an increase in tenderness during excursion of the mandible.

Disturbance in the occlusal relationship of the teeth is commonly present. Fractures complicated by overriding shorten the distance between the angle and the mandibular fossa. In unilateral fracture, the posterior teeth on the affected side are brought into premature contact, thus producing an open bite on the opposite side in the anterior region. Frequently a retro-occlusion of the posterior mandibular teeth is found on the affected side. When the mouth is open, the distance between the occlusal surfaces is less on the affected side than on the normal side. The chin will also be displaced toward the affected side. Bilateral condylar fractures with upward and posterior displacement of the mandible produce premature contact of the posterior teeth and an open bite anteriorly; in such cases, protrusive excursion of the mandible is impossible. An important method of diagnosing these fractures is to place the index fingers in the auditory canals. Normally, the condyle can be clearly felt here when the mouth is opened and closed. When a fractured condyle is dislodged from the mandibular fossa, these movements are less distinct. When it is dislodged from the capsular ligament, the movement cannot be felt at all. Hemorrhage from the ear may mean that the fractured condylar head may have fractured the tympanic plate. This can be very serious.

TREATMENT

The treatment of condylar fractures must be based on diagnostic facts. Accurate roentgenograms showing the fracture line and positions and relations of the fragments are important to the study of the problem. The condition of dentition, disturbance of occlusion, and dysfunction of the mandible during excursion must be considered in planning the treatment. Since condylar fractures are commonly associated with other mandibular fractures, combined evaluation and management are often necessary. The aims of treatment in all mandibular fractures are the restoration of normal function with correct occlusion, or correct interarch relations if the patient is edentulous, and the elimination of the associated deformity. Early reduction and immobilization favor a satisfactory result.

Closed reduction.—Closed reduction and immobilization is a form of treatment that has many modifications varying with the specific

problem. If there is little or no displacement and relatively free movement of the mandible, early immobilization by some form of intermaxillary fixation is advocated for 3 to 5 weeks. When displacement or dislocation is evident, an attempt at reducing the condylar fragment is indicated before immobilization. This is particularly important if excursions of the mandible are blocked by the malposed condylar head. Reduction may be attempted by bimanual manipulation extraorally and intraorally. If overriding is present, downward traction on the ascending ramus will permit the return of the condylar fragment to a more normally functioning position. Such manipulative procedures are more efficacious if a general anesthetic is administered to the patient, because displacing forces are released by complete muscular relaxation. When there is overriding of fragments, resulting in an anterior open bite, the muscle spasm may be gradually overcome by anterior intermaxillary elastic traction. With this procedure the posterior opposing teeth act as a fulcrum, while the anterior bite is closed and normal space is restored for the overriding fragments. This principle is employed in the use of posterior bite plates, blocks, and appliances in edentulous posterior areas in order to increase the fulcrumlike action. With the relaxation of the muscles of mastication and restoration of adequate joint space, the condylar fragment may be reduced to a more normal position. The goal of manipulative procedures in such cases is not an accurate anatomic coaptation of fragments but an approximate alinement which does not inhibit mandibular excursions.

The type of immobilization and period of fixation are variable phases of conservative treatment. After manipulative reduction, and assurance that mandibular excursion is not blocked by condylar displacement, some form of fixation may be applied. Among the appliances used for intermaxillary fixation are: (*a*) direct interdental wire ligation; (*b*) wire lug-forming devices of the Stout or Risdon type; (*c*) buttons; (*d*) arch wires; and (*e*) splints provided with lugs for intermaxillary elastic traction. Each of these appliances is specially designed for a specific type of case. Care must be exercised to minimize irritation to soft tissues and to prevent unbalanced displacing forces on the teeth. The most satisfactory appliance is that which distributes the forces of traction evenly over the supporting dentition with the least damage to periodontal structures. It is generally agreed that fixation should be applied as soon as possible after manipulation of the mandible has restored normal closed occlusion. Closed fixation may be delayed temporarily from 24 to 48 hours while intermaxillary elastic traction produces the desired reduction. Incomplete fixation has been advocated by those who contend that fragment mobility will prevent threatened ankylosis. Early limited excursions are encour-

aged in order to establish a flail joint or pseudarthrosis. According to this concept, an adaptive balance of the muscles of mastication permits adequate functional excursions in such a condition. This principle is preferred by some British authorities for treatment for unilateral condylar fractures. Cap splints which embrace training flanges are frequently cemented to the teeth for guidance of the mobile mandible to proper occlusion.

The management of bilateral fractures of the condyle does not differ significantly. Since typical posterior displacement of the mandible and anterior open bite are often extensive, early and complete reduction and immobilization are advantageous in preventing serious deformity. Sometimes anterior and superior traction may be applied by intermaxillary elastics. When reduction is complete, immobilization is established and maintained for the desired period. The period and degree of fixation will vary with the patient and with the viewpoint of those in charge.

Intracapsular fracture of the condylar head is relatively rare and difficult to demonstrate. Some authorities have designated intracapsular fractures involving articular joint surfaces as those most vulnerable to ankylosis. Treatment by conservative methods is essentially the same as that in other condylar fractures. Since fractures of the condyle are so frequently associated with other mandibular fractures, intermaxillary fixation provides a combined form of treatment. Under these conditions, a compromise must be made between the ideal fixation periods for each fracture. It is considered advisable to continue observation of patients with condylar fracture for 4 to 6 weeks after discontinuing fixation. Minor adjustments in articulation of the teeth may be indicated and are readily made by selective grinding.

Open reduction.—In recent years open reduction of fractures of the condyle has been advocated by those who believe that dislocation and appreciable displacement are indications for surgical intervention. The procedure has ranged from reduction through a simple intraoral or extraoral incision to a complex visual reduction with transosseous wire ligation of fragments in exact anatomic relation. The intraoral approach employs a vertical incision 2 cm. long from the tip of the coronoid process inferiorly along the anterior border of the ascending ramus (*2*). Soft tissues are reflected from the medial surface, and a urethral sound is inserted to engage the medially displaced fragment and reduce it laterally by lever action. The buccal maxillary tuberosity serves as the point of the fulcrum. When the condylar head is reduced, intermaxillary fixation is applied. A similar manipulative procedure may be performed with a small hook through a short horizontal preauricular incision just inferior to the zygomatic arch (*3*).

Difficulties are encountered in performing a complete open reduction and fixation. Through a vertical preauricular incision, adequate visibility and exposure are difficult; in a small, deep field one must accomplish a difficult technical procedure without damage to such important adjacent structures as the internal maxillary artery, branches of the facial nerve, and the temporomandibular joint capsule; fixation is laboriously complex with this approach. Wire ligation through holes drilled in the approximated fragments is sometimes considered ideal fixation. In selected cases, external pin fixation has been used to supplement internal wiring. Pins are inserted just below the condylar head and into the temporal zygomatic process. More radical surgical management employs condylectomy in cases involving wide displacement and dislocations. Several unsuccessful attempts at open reduction have necessitated condylectomy.

All methods of open surgical reduction are combined with some form of intermaxillary fixation. Patients are selected for open reduction when it is considered that they will not respond well to a closed procedure. Advocates of the open procedure emphasize various complications such as ankylosis, traumatic arthritis, limited motion, and malocclusion that may arise when the closed method is used. They suggest that we are not aware of these complications because clinical cases that have been reported were managed by conservative methods and have not been followed closely for years after treatment.

Ivy (*4*), Berger (*5*), and many others have stressed the fact that without realinement of fragments, condylar fractures under conservative treatment attain satisfactory functional results. Open operation has not been widely used for many reasons. There are numerous types of condylar fracture in which open reduction and fixation is a technical impossibility. The procedure predisposes to many complications. The fracture is made compound by the procedure, and additional invasion of, and trauma to the joint capsule foster cicatricial processes and ankylosis. Surgical intervention is dangerous because of the proximity of the fracture to several important structures. Direct wiring and pin fixation induce trauma and introduce foreign material, thereby inviting infection and necrosis. Most authors, therefore, prefer the closed reduction technique. Thoma is the greatest advocate of the open reduction method. He has observed satisfactory results in many patients. Other writers, however, cite many more that were treated conservatively with excellent results (*3*).

In reviewing 155 case histories, I found that about 145 of them were treated conservatively and the remainder by different types of open reduction. I was surprised to find that the patients treated conservatively obtained excellent results, even when displacement was present. The following are some recent case histories of fractures of the man-

dibular condyle that were treated at the dental clinic of Walter Reed General Hospital. All of these patients were treated conservatively.

CASE REPORTS

Case 1.—The patient reported to the dental clinic with swelling of the right side of the face just anterior to the tragus of the ear and pain on moving the jaw. The mandibular excursions deviated little from the normal. A diagnosis of simple complete fracture of the neck of the condyle of the right mandible was made. Roentgenograms confirmed the diagnosis. Using 2 percent procaine locally, intramaxillary loop wiring and intermaxillary elastic traction were applied. Occlusion was established without difficulty. The patient was seen daily for irrigation of the oral cavity and adjustment of the tractor. All pain disappeared from the fracture site within a week. After 2 weeks all traction was removed and the patient was able to accomplish all mandibular movements without pain. Two days later all wiring was removed. There was good function, no pain, and no deformity.

Case 2.—The patient reported to the dental clinic with pain in the region of the left temporomandibular joint, swelling, and a deviation of the occlusion to the left. Roentgenograms disclosed a simple, complete fracture at the neck of the condyle of the left mandible. Intramaxillary wiring with intermaxillary elastic traction was applied. After 5 days the normal occlusal relationship had been re-established and all pain had disappeared. Traction was removed on the eighth hospital day and six days later the wiring was removed. There was no deformity.

Case 3.—The patient was sent to the dental clinic with a diagnosis of a fractured mandible. The fracture had occurred 1 week previously. Examination disclosed an edentulous upper arch with a full denture in place. The lower molar teeth were missing. There was a deviation from the normal occlusion and pain in both temporomandibular areas when the mandible was moved. Roentgenograms disclosed simple, complete fracture of the right mandible at the mental foramen, and at the neck of the condyle, and simple, complete fracture of the left mandible at the neck of the condyle with medial displacement from the glenoid fossa. Occlusion was re-established to the upper denture and the lower jaw was stabilized by means of a head cap and flexible collodion chin plate attached by elastic traction. After 8 days the occlusion was normal and no pain was felt when the jaws were opened. Two weeks later all stabilizing aids were removed. There was good bony union but the denture was no longer satisfactory and the patient required new complete upper and partial lower dentures.

Case 4.—The patient was sent to the dental clinic with roentgenographic evidence of simple, complete fracture of both mandibles at the neck of the condyle, with displacement, and simple, incomplete fracture of the symphysis of the right mandible. Intramaxillary continuous wire loops were applied, the fractures were reduced, and elastic traction was applied. L–12 was fractured and extracted. A good result was obtained.

Case 5.—The patient was brought to the dental clinic following a jaw injury. Examination disclosed a deviation to the left when opening the mouth. There was swelling anterior to the tragus of the left ear and pain on palpation. A diagnosis of simple, complete fracture of the left mandible at the neck of the condyle was made. Roentgenograms confirmed the diagnosis and showed the head of the condyle to be displaced medially from the glenoid fossa. Intramaxillary wiring was applied with intermaxillary elastic traction to re-establish the normal

relationship of the teeth and jaws. The patient was seen daily for irrigation of the oral cavity and adjustment of the tractor. After 2 weeks there was very little loss of function and no further treatment was deemed necessary, although because of nonunion it was believed that resection might become necessary later. After 23 days all traction was removed. Function was excellent and the patient had no pain or discomfort.

Case 6.—The patient was sent to the dental clinic because of a fracture of the mandible which had occurred several days previously. Examination disclosed a fracture of the symphysis of the mandible with distal displacement of the right side signifying probable fracture of the condyles. The maxilla was slightly mobile, but was not displaced. Roentgenograms disclosed (*a*) compound, complete fracture of the symphysis of the mandible; (*b*) simple, complete fracture of the neck of the condyle of both mandibles; and (*c*) fracture of the maxilla with cicatricial tissue union and no displacement. Impressions were obtained for the construction of a splint. Penicillin in doses of 300,000 units daily was given for 5 days. On the third hospital day the fractures were reduced and the splint applied. Intramaxillary wiring was applied to the maxillary teeth and occlusion was established with elastic traction. One week later the occlusion was normal. Thirty-three days after traction was applied it was removed. Roentgenograms taken at that time showed good alinement of the fractures and some callus formation. Seventeen days later the splint was removed. The occlusion was adjusted to provide a better cuspal relationship. There was no deformity or loss of function.

Case 7.—The patient reported to the dental clinic with injuries received 2 days previously. Examination and roentgenograms disclosed: (*a*) compound, comminuted fracture of the maxillary alveoli from L–3 to R–5; (*b*) fracture of the teeth L–1, R–1, R–2, R–3, and R–4; (*c*) compound fracture of the anterior one-third of the palatine bones with posterior displacement; (*d*) complete, compound fracture of the left mandible in the region of the mental foramen; and (*e*) fracture of the neck of the condyle of the left mandible displacing the condyle medially out of the glenoid fossa. The mandible was manipulated under local anesthesia in an attempt to replace the condyle without success. The fractured teeth were extracted and the loose pieces of alveolar bone were removed up to and including the anterior concave portion of the vomer. Hemorrhage precluded the removal of two root tips of R–4 at this time. The palatine bones attached to the mucoperiosteum of the palate were placed in position and the soft tissues were sutured. Impressions were obtained for a maxillary splint. A gauze pack was then placed against the palate and held under pressure by wires from the bicuspid teeth. Continuous loop wiring was applied to the mandibular teeth. A head bandage was then applied to stabilize the jaws and the patient was returned to the ward. After 3 days the upper splint was applied. Traction was placed so as to create space for the condyle to be returned to the glenoid fossa. Two days later it was apparent that the condyle was not being reduced, so normal occlusion was established and elastic traction was applied to maintain this position. The patient was seen daily for irrigations of the oral cavity and adjustment of the tractor. Two weeks after traction was applied it was removed, and 2 days later the splint was removed. The vertical opening was excellent as were the left lateral and protrusive excursions. There was limitation of the right lateral excursion. There was apparently no impingement on any nerves by the misplaced condyle. On the next day the residual roots were located and removed, and 3 days later all wiring was removed. It was estimated that 6 more weeks would be required before an upper partial denture could be made. The left

condyle was still detached but did not interfere with normal masticatory movements of the mandible and no treatment was deemed necessary at the time of discharge from the clinic.

Case 8.—The patient was brought to the dental clinic where roentgenograms disclosed a simple, complete fracture of the neck of the condyle of the right mandible. The condyle was displaced upward and inward. Intramaxillary elastic traction was applied for reduction and fixation of the fracture. Eighteen days later the wiring was removed. The fracture was healing in normal position at this time. There was no disability, deformity, or loss of function.

SUMMARY

Fractures of the condyle have been classified according to the displacement or dislocation of the condylar fragment. The prime objective of treatment is the restoration of normal function and the elimination of any associated deformity. Conservative methods of reduction and intermaxillary fixation are simple and effective.

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Toxicity of Intrathecal Penicillin

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IN THE past few years, reports on the toxicity of intrathecal penicillin have been increasing (*1*) (*2*) (*3*) (*4*) (*5*) (*6*) (*7*) (*8*) (*9*). A case of toxic reaction accompanying penicillin therapy is presented.

CASE REPORT

A 5-year-old girl entered a station hospital in Japan on 9 August 1947 with a history of sore throat, fever, headache, and malaise of 4 days' duration. One day prior to admission she had generalized muscular aches, associated with pain and stiffness of the neck.

Physical examination at this time revealed an acutely ill child with a temperature of 103° F., stiff neck, and a positive Kernig's sign bilaterally. The spinal fluid was clear and the cell count was 138, 90 percent of which were polymorphonuclear leukocytes and 10 percent were lymphocytes. Pandy's test was positive, and the sugar was 45 mg. per 100 cc. A tuberculin skin test was negative.

Since there was an epidemic of poliomyelitis in that area, a diagnosis of preparalytic poliomyelitis was made. Bacterial meningitis was considered in the differential diagnosis because of the low spinal fluid sugar and the differential leukocyte count in the spinal fluid.

She was immediately given a single dose of 20,000 units of penicillin intrathecally and 4 gm. of sulfadiazine orally. She was also given 30,000 units of penicillin intramuscularly every 3 hours. The day after admission, although she was alert and active and exhibited no signs of systemic toxicity, there were definite signs of meningeal irritation. The sulfadiazine dosage was increased to 6 gm. daily, and on the third hospital day a second lumbar puncture was performed; the spinal fluid was clear, the pressure normal, and no cells were reported; the smear, culture, and Pandy's test were negative. Because of the possibility of a bacterial meningitis 50,000 units of penicillin were given intrathecally. The temperature, which had fallen, rose again to 103° F. and the patient became irritable, vomited, and showed definite signs of meningeal irritation. On the fourth hospital day the signs of meningeal irritation decreased. Gross hematuria was present and the fluid intake was increased to 3,000 cc. daily. The temperature remained slightly elevated.

On the fifth hospital day a third lumbar puncture was performed. The spinal fluid cell count was 10, 7 of which were lymphocytes and 3 were polymorpho-

[1] Letterman General Hospital, San Francisco, Calif.

nuclear leukocytes. An intrathecal injection of 50,000 units of penicillin was given: within 3 hours she had a severe headache, back pain, and a hydrocephalic cry, stiff neck, and irritability alternating with drowsiness. The temperature rose to 105° F. and all deep tendon reflexes disappeared. It was then considered that the changes in the spinal fluid cell count and the fluctuation in the severity of the central nervous system symptoms were caused by a brain abscess.

Ten hours after the third lumbar puncture, on the same day, a fourth lumbar puncture was performed. The fluid was turbid and the cell count was 7,200, 75 percent of which were polymorphonuclear leukocytes and 25 percent were lymphocytes; Pandy's test was strongly positive, and the sugar was 40 mg. per 100 cc. This appeared to be further evidence of the hypothesized brain abscess, and another 50,000 units of penicillin were given intrathecally. The patient vomited following this treatment and had extreme nuchal rigidity. She was given a transfusion of 250 cc. of citrated blood and 250 cc. plasma. On the sixth hospital day parenteral fluids were administered because of continued temperature elevations which reached a peak of 107° F. At this time the patient had two generalized convulsions each lasting a few minutes, involving the face and the upper extremities. Neurologic examination revealed absent abdominal reflexes bilaterally. Babinski's test was positive on the left, the knee jerks were hyperactive, and ankle clonus was present on the left. Extreme nuchal rigidity and positive Brudzinski's and Kernig's signs were noted bilaterally. Spasticity was present in the calf muscles bilaterally. These findings were definitely thought to be caused by brain abscess. On the seventh hospital day a cisternal puncture was done and the cell count of the fluid was 544, 68 percent of which were polymorphonuclear leukocytes and 32 percent were lymphocytes. Thirty thousand units of penicillin were instilled cisternally. On the eighth and ninth hospital days repeated lumbar punctures were performed and 30,000 units of penicillin were instilled intrathecally on each occasion. The cell count of the cerebrospinal fluid continued to be elevated and signs of meningeal irritation persisted.

She was transferred to an Army general hospital in Japan on the tenth hospital day. On admission she was found to have slight nuchal rigidity. A lumbar puncture revealed clear spinal fluid with a cell count of 5, all lymphocytes; the smear and culture were negative. Penicillin intrathecally and sulfadiazine were discontinued but penicillin was continued intramuscularly. On the twenty-third hospital day sulfadiazine was again administered because of the possibility of a brain abscess. Throughout her course in the hospital, the patient's temperature gradually decreased. She remained alert and active. Her temperature remained normal after the twenty-second hospital day. Penicillin was discontinued on the thirty-first and sulfadiazine on the thirty-seventh hospital day. The patient was admitted to this hospital 47 days after her original hospitalization for further study to rule out a brain abscess. On admission she was alert and afebrile, there were no abnormal neurologic findings, and an electroencephalogram was normal. When last seen, in June 1949, the patient was asymptomatic.

COMMENT

The patient was seen by a member of the United States Army Virus Commission who considered her early history to be compatible with a diagnosis of preparalytic poliomyelitis. He stated that the low spinal-fluid sugar concentrations were compatible with those of most of the

patients he had seen in the current epidemic in Japan. He recommended discontinuing the sulfadiazine because of the danger of renal damage and that the patient be removed to a general hospital for observation for a brain abscess. It was believed that the intensive intrathecal therapy with penicillin contributed to her fever, increased her spinal fluid cell count, and produced signs of meningeal and central nervous system irritation.

DISCUSSION

Absorption rates of penicillin given intramuscularly.—Early clinical investigation has revealed that parenteral administration of penicillin does not result in its excretion into the subarachnoid space of normal persons in bacteriostatic concentrations (*1*) (*10*). Some penicillin was found in the cerebrospinal fluid 31 hours after parenteral injection but not in effective concentration (*11*). It was absorbed more readily and produced higher concentrations when given parenterally in patients with meningitis if the infection was acute (*12*). In patients with chronic low-grade meningitis, parenteral injections did not result in effective concentrations of the drug in the cerebrospinal fluid (*11*). In those with acute meningitis, a bacteriostatic level of penicillin in the cerebrospinal fluid could not be attained for more than 1½ hours by parenteral administration. To attain such levels, large amounts (500 to 5,000 units per kg. of body weight) were required and even then the levels obtained were quite variable (*13*). There was no assurance that the patient would attain a beneficial titer of the bacteriostatic agent in the cerebrospinal fluid, since the absorption of the same amount was unpredictable after repeated administrations. Thus, direct instillation of penicillin into the subarachnoid space was necessary if high levels were desired in treating infections of the meninges caused by susceptible organisms.

Dosage schedules recommended.—It was noted early in the literature that administration by such a route would result in harmful reactions. In 1944 a report appeared suggesting that penicillin had detrimental effects on the central nervous system after intrathecal instillation (*3*). Prior to this, Rammelkamp and Keefer (*1*) advocated that penicillin be given intrathecally, but in dosages not exceeding 3,000 to 5,000 units daily because of the possible occurrence of pleocytosis in the cerebrospinal fluid after large doses.

Other writers recommended intrathecal doses of never more than 10,000 units daily, but reports again began to appear showing that penicillin was being used in larger amounts (*3*) (*14*). Each report illustrated that penicillin acted on the meninges as an irritating foreign body and produced many undesirable effects. The lowest reported intrathecal amount to cause signs of meningeal reaction was

18,000 units (*3*) (*15*). The largest amount recorded as having been used in a single intrathecal injection was 300,000 units (*16*). This was followed by symptoms compatible with severe adhesive arachnoiditis, which was later proved at craniotomy.

Specific toxic reactions in man.—Although the previously mentioned cases and an increasing number of others have appeared in the literature in the past 5 years, it appears to be necessary to call attention to the reactions that occur when the drug is used intrathecally. These reactions have included: (*a*) damage to the cauda equina and spinal cord (*17*); (*b*) flaccid and spastic paralysis of the extremities (*15*); (*c*) status epilepticus (*18*); (*d*) adhesive arachnoiditis (*16*); (*e*) transverse myelopathy (*6*); (*f*) sacral radiculitis (*8*); (*g*) convulsive seizures (*18*) (*19*) (*20*); (*h*) optic atrophy (*3*); (*i*) general signs of meningeal irritation (*2*) (*4*) (*7*) (*9*) (*21*); and (*j*) pleocytosis of the cells in the spinal fluid (*5*) (*22*). The symptoms and signs that may be produced are shown in table 1. Most of the experimental work has been done on the convulsive effects of penicillin given intrathecally (*19*) (*23*) (*24*). The effective bacteriostatic agent in penicillin is itself responsible for the convulsions produced. Certain impurities that cause pyrogenic reactions do not appear to cause the convulsions.

Whether the convulsions that occurred in our case could be attributed directly to the use of the drug or whether they resulted from the febrile reaction cannot be definitely stated, but it would appear that the penicillin was a contributing factor.

TABLE 1.—*Symptoms and signs following intrathecal administration of penicillin*[1]

General:	Neurologic:
Fever.	Convulsions.
Headache.	Paresthesia.
Irritability.	Facial nerve palsy.
Listlessness.	Loss of speech.
Cardio-respiratory:	Nuchal rigidity.
Vascular collapse.	Paralysis of extremities.
Irregular respiration.	Muscular fibrillation.
Gastrointestinal:	Muscular spasm.
Nausea.	Signs of pyramidal tract irritation.
Vomiting.	Incontinence of urine.
	Abnormal electro-encephalogram.
	Pleocytosis and increased globulin in the spinal fluid.

[1] Adopted from Morginson (*21*).

CONCLUSIONS

1. The safest dosage of penicillin given intrathecally appears to be not over 10,000 units daily.

2. Toxic reactions are to be expected if dosages above this level are used.

3. Penicillin should not be used intrathecally unless specifically indicated.

4. It is apparent that the stormy clinical course in the case reported was caused by the repeated intrathecal administration of penicillin. There was no sound indication for the intrathecal administration of penicillin in what was presumably preparalytic poliomyelitis.

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Mosquito Control Problems in Japan

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MALARIA, filariasis, dengue, and Japanese encephalitis are the mosquito-borne diseases of man known to occur in Japan. Malaria was not a reportable disease in Japan prior to Allied occupation and the information available on its incidence and distribution does not permit accurate evaluation of the problem over a period of years. The statistics compiled by the Public Health and Welfare Section, Supreme Commander for the Allied Powers, show about 11,000 cases of malaria among the Japanese in 1947, and 4,752 cases in the first 11 months of 1948. Cases were reported from all Prefectures of the country in both years for which complete records are available. About one-half of the cases reported in 1948 occurred in Shiga Prefecture in south central Honshu and the remaining cases reported showed a rather even distribution throughout the four principal islands. This distribution strongly suggests that, except for Shiga Prefecture, a large number of cases of malaria are occurring among repatriates and returned Japanese soldiers who contracted the disease elsewhere. This conclusion is further supported by the fact that the total number of cases reported in 1947, when repatriation was continuing at a high level, was more than double the number reported in 1948. All information at hand supports the contention that malaria does not constitute a significant public health problem in Japan.

No significant filariasis surveys have been conducted among the Japanese to date by Allied Medical Department personnel. In three separate areas on south central Honshu, malaria survey detachments made about 1,000 thick smears on adults and in this series only 1, that of a Chinese who had resided most of his life in southern Malaya, was positive for filariae. The latest extensive surveys performed by

[1] 207th Malaria Survey Detachment.

Japanese workers were made in 1926 among soldiers of the Japanese Army. Endemicity for filariasis in the latter studies varied from 0 to 2 percent in Prefectures in the southern half of Honshu while on the southernmost island of Kyushu, infection rates varied from 0.5 to 12 percent in the Prefectures in which surveys were made. The highest rates recorded were along the western and southern coasts of Kyushu. More up-to-date surveys, accomplished under carefully controlled conditions are in order at present and a new appraisal of the problem would be the only basis on which to evaluate the relative importance of this disease from a public health point of view.

According to Japanese informants, dengue was unknown in Japan prior to 1942. There is no evidence to back this claim other than a record to this effect contained in an unpublished paper made available by a member of the teaching staff at Kyoto University. Data enumerated here were obtained from the latter source. In 1942 an epidemic of about 13,000 cases of dengue occurred in Nagasaki, Kyushu, and in 1943 over 10,000 cases were recorded in the Kobe-Osaka-Kyoto area in south central Honshu. In 1944 and 1945 fewer cases were seen and these were also limited largely to the epidemic area of 1943. No cases have been recorded in Japan since 1945. Dengue outbreaks from 1942 through 1945 were of about 7 weeks' duration beginning in late July and terminating shortly after mid-September. The benign nature of this disease and the present lack of evidence of its actual establishment on these islands serve to relegate it to a secondary position in the mosquito-borne disease problem.

From the standpoint of case incidence, severity, and geographic distribution, Japanese encephalitis is the most important mosquito-borne disease in Japan. Outbreaks that were probably Japanese encephalitis date back to 1871, but the first large epidemic on record occurred in 1924. Over 6,000 cases were recorded in that year. Another epidemic involving over 5,000 cases occurred in 1935, followed by the largest outbreak on record in 1948 with 8,023 cases and 2,455 deaths, giving a case fatality rate of about 30 percent while the case fatality rates in previous epidemics ranged as high as 60 percent. In the years between 1935 and 1948 the incidence varied from a few cases to 2,800 with some cases occurring almost every year. About 33,000 cases are on record from 1924 through 1948. The figures quoted make no allowances for patients who may have been misdiagnosed.

In the 1948 outbreak there were 30 cases of the disease with 5 deaths among occupation personnel. No figures showing the occurrence of the disease in immunized persons were available. This disease appears regularly from year to year in the south central portion of Honshu in the inland-sea area, and while it occurs particularly in epidemic

years in all islands of the archipelago it is rarely seen in the northernmost island of Hokkaido. Serologically it can be shown that a large proportion of the indigenous population has had experience with the virus. It is estimated that the ratio of clinically recognizable cases to inapparent infections is between 1 : 300 and 1 : 1000. Thus, we have a disease that is practically nation-wide in distribution, a fact which is important in considering mosquito control as a means of protecting the population.

IMPORTANT VECTORS

There are about 50 species of mosquito in Japan but of this number not more than 8 are important from the standpoint of their feeding habits. Among those which feed on man readily are *Culex pipiens pallens*, *C. tritaeniorhynchus*, *C. bitaeniorhynchus; Aedes albopictus*, *A. flavopictus*, and *A. vexans nipponii*, all of the latter being important day-biting mosquitoes. *Anopheles hyrcanus sinensis* is the only important anopheline and is the vector of malaria in Japan. In certain sections of the country a representative of the genus *Mansonia* occurs and it is a severe pest in the localities where it is established.

Japanese workers claim to have isolated the virus of Japanese encephalitis from *C. tritaeniorhynchus* in nature and the evidence at hand points to this species as the principal vector of the disease. *C. pipiens pallens*, a closely related species, is claimed, on the basis of studies carried out by Japanese, to carry the virus in nature and its habits and seasonal incidence strongly incriminate it as a possible vector. *A. albopictus* is the most likely vector of dengue. Filariasis may be transmitted by any of the mosquitoes which feed on human beings since the entire group has been proved experimentally to be capable of transmitting this disease.

The composite list of breeding sources of mosquitoes that readily feed on man in Japan is most impressive and emphasizes the difficulty of control. Most important species live in close proximity to human habitation and practices associated with agricultural pursuits create a large proportion of mosquito-breeding habitats. An understanding of the basic problem entails a knowledge of local agricultural practices. Rice constitutes the principal agricultural crop of the country. The rice paddies are flooded in June and remain under water throughout the breeding season of the important species of mosquito. In addition to the paddies, rice-growing districts are heavily interlaced with a system of drainage and irrigation ditches containing stagnant or slowly moving water. Night soil constitutes a large part of the fertilizer employed in growing crops and the tanks used for storing it dot the landscape wherever crops are grown. In the application of night soil as fertilizer large quantities of water are used. Thus

we have a large portion of the land under water and productive of some mosquitoes through the summer months, mosquito-producing rice paddies in abundance, and night-soil storage and garden-irrigation tanks scattered throughout the rural areas serve to further augment the mosquito population. To these can be added poorly constructed roadside ditches, gutters, and, occasionally, extensive unreclaimed marshy areas. A few of the smaller breeding sources include innumerable artificial containers such as drums, bowls, buckets, cans, urinal crocks, flower pots, decorative stone vases, native latrines, cisterns, water-holding rubble in bombed areas, and the stumps and posts of cut bamboo. Thus we have a diverse and extensive breeding problem presenting a difficult approach from a control standpoint.

Temperature and rainfall have a determining influence on mosquito propagation. The daily high temperature normally reaches 70° F. about the beginning of May in all areas of Japan south of Tokyo, at or near sea level. There is a gradual increase in daily mean temperatures from May to late June at which time daily high readings are between 80° and 85° F. In early July daily temperatures reach 90° to 95° F. and this level is maintained to the end of August. June and September are usually the wettest months but there is no true wet or dry season in Japan. Seasonally the first heavy impetus to propagation of mosquitoes is given by the higher temperatures attained in the latter part of June coupled with heavy precipitation occurring in that month. There is a steady upward climb of the density curve of biting species through July with a peak usually attained by mid-August. A great decrease in mosquito density occurs in the latter part of August and with the onset of cooler weather in September the density quickly approaches zero. The mosquito-control program requires close attention in the field from about mid-May through mid-September in the area extending south from Tokyo. A mosquito-control program must be based on a knowledge of the mosquito-borne diseases present in a given area, their relative endemicity or epidemicity largely determining the amount of time and money to be expended. In some parts of the world the degree of discomfort occasioned by pest mosquitoes or economic considerations determine the appropriation of funds for abatement projects. In Japan, any or all of these factors may be considered, depending on the time of the year, seasonal variations in the intensity of mosquito activity, geographic location, and the presence in some seasons of mosquito-borne epidemics.

About 30 percent of the land in Japan is arable and the populated areas coincide closely with areas potentially productive agriculturally. Similarly the mosquito-control areas coincide closely with the arable land since the remainder of the country is mountainous and sparsely

populated. The total land area of Japan exclusive of Hokkaido is 113,000 square miles. The 30 percent which is populated represents an area of about 34,000 square miles that would require coverage at 10-day intervals over a period of at least 4 months each year, if abatement were to be successful. It is, therefore, doubtful whether abatement on a nation-wide basis, exclusive of the northernmost island of Hokkaido, is feasible. Public health is purchasable, for a price, but the cost of this phase would probably be too great to be justified by the resulting improvement in health. The long-term plans for expenditures of public funds for mosquito-abatement programs in Japan must be economically sound, and must be capable of successful accomplishment.

Some indication of the relative success we have met this far in control operations may be deduced from field survey data obtained over several years. Human beings were used as bait and capture of adult mosquitoes were made as they settled on their victims. Biting intensity records were made at 3- to 4-day intervals between 1900 and 2300 hours from late July to the end of the first week in September in 1946 and 1947. A large city of over a million inhabitants and a typical rice-growing district were selected for study since these areas afforded an opportunity for comparison of population densities in typical urban and rural localities. During 1946, in the urban area, biting intensities varied from an average hourly low of 6 to a high of 35 per hour and throughout August the average biting rate never fell below 20 in all hourly periods recorded. During the same year in the rural area biting rates varied from an average low of 20 to a high of over 100 per hour. Similar observations at the same collection points were made in the summer of 1947. While the biting rates were slightly lower in 1947, the extent of reduction was not significant.

During July and August 1948 large numbers of resting adult females were collected in the vicinity of Okayama in southern Honshu and frequently a single stable yielded several thousand mosquitoes. Stables were usually small and seldom sheltered more than a few domestic animals. Similarly, light trap collections made in the same area yielded from 500 to over 1,000 mosquitoes in a single night's catch. These figures indicate that despite the control program, a sufficient mosquito population was maintained to present a serious pest or disease vector problem if mosquito-borne diseases had made their appearance.

All of the factors underlying the 1948 outbreak of Japanese encephalitis, the largest in the history of Japan, are not known. While it is possible that the magnitude of the outbreak could reflect a breakdown in efficiency of mosquito-control operations as compared with the 2 previous years, it is doubtful on the basis of previously cited data

that an outbreak of the same magnitude might not have occurred sooner had other requisite factors occurred. We must recognize the fact that in the third year of the mosquito-control program in Japan its inadequacy in controlling Japanese encephalitis was evident. So far only the surface in effective mosquito eradication has been touched even in the large urban centers of population. In smaller communities and rural areas the situation is probably much the same as it was prior to the war. The progress made represents a beginning but the task ahead is tremendous if the ultimate goal is mosquito control, limited even to the larger population centers.

A Method for Testing Sensitivity of Organisms to Antibiotics

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THE clinical effectiveness of penicillin is paralleled by the sensitivity of the invading organisms in vitro (*1*) (*2*). The efficacy of penicillin in the treatment of infection may be accurately determined by testing the sensitivity of the organism in vitro (*3*). Penicillin K is more active in vitro than in vivo (*4*). This fraction has now been largely eliminated from commercial preparations. A similar parallelism between in vitro and in vivo activity has been shown for streptomycin. These facts have been reviewed and summarized recently by Keefer (*5*) and Goldstein (*6*). Sensitivity tests on organisms are desirable if the proper antibiotic is to be prescribed in the optimal dosage. Frequently, an organism that shows a high degree of resistance to penicillin will be found to be sensitive to streptomycin. The sensitivity spectra of organisms isolated from human infections have thus become as important as their isolation and identification. Goldstein emphasizes the importance of frequently determining organism sensitivity and, as far as possible, increasing the dosage of the antibiotic to meet new thresholds.

Penicillin sensitivity test.—A stock dilution of penicillin potassium containing 20 units per ml. is prepared in sterile physiologic saline solution. The following dilutions are then prepared: 10, 5, 2.5, 1.25, 0.62, 0.31, and 0.15 units per ml. One milliliter of each dilution is added to a sterile labeled Petri dish to which is then added 9 ml. of melted and cooled tryptose blood agar with a *p*H of 6.8. The contents of each Petri dish is mixed before solidification by gentle clockwise and counterclockwise rotation. Plates may be stored in the refrigerator for not more than 24 hours before use. The final concentrations represented by these plates are: 1, 0.5, 0.25, 0.125, 0.06, 0.03, and 0.015 units per ml.

[1] Oliver General Hospital, Augusta, Ga.

Well-isolated colonies of organisms to be tested are transferred from diagnostic plates to small test tubes containing about 1 ml. of tryptose phosphate broth to which has been added a loopful of sterile, Seitz-filtered, human serum. These booster broth tubes are incubated at 37° C. Control cultures of *Staphylococcus aureus* (Heatley, Eden, or F. D. A. 209P) are set up at the same time. In this laboratory, a culture of a penicillin-resistant staphylococcus is also prepared.

A sterile cotton swab is saturated with the booster broth culture after incubation for 4 to 6 hours. Excess medium is squeezed from the cotton tip against the side of the tube. A sector of each penicillin plate and of a control plate without penicillin is inoculated with the swab, making a single line streak on each plate, working from the plate containing the lowest to the one containing the highest concentration, inoculating the control plate first. Separate sectors are thus inoculated with various organisms to be tested. Six organisms can be conveniently tested on a single set of plates. Each set should also be inoculated in sectors reserved for the control organism. The results are read after overnight incubation. Growth or lack of growth is recorded for each organism on each plate. The sensitivity is then reported as the lowest concentration at which growth is completely inhibited.

Streptomycin sensitivity test.—The stock solution for the streptomycin sensitivity test contains 640 micrograms per ml. The following dilutions are then prepared in physiologic saline solution: 640, 320, 160, and 80 micrograms per ml. Plates prepared in the manner previously described are used, except that the agar base is adjusted to a *p*H of 8. The final dilutions represented by four plates are 64, 32, 16, and 8 micrograms per ml. Preparation of the organisms to be tested, inoculation of the media, and reading of the results are similar to that described for the penicillin sensitivity test. *Proteus OX19* may be used as a control organism. The cultures of this organism employed here do not grow on the lowest concentration of streptomycin used.

DISCUSSION

Routine sensitivity testing of isolated organisms may be adjusted to meet local needs. Beta-hemolytic streptococci from sputa, wounds, abscesses, pleural fluids, urine, blood, and aural discharges are tested for sensitivity to penicillin, and if found to be resistant, are tested for sensitivity to streptomycin. Staphylococci are treated similarly. Gram-negative rods are tested for sensitivity to streptomycin only. Such organisms as *Neisseria gonorrhoeae* and *Diplococcus pneumoniae* are not routinely tested because they are regularly sensitive. Organisms that require special growth factors or atmospheric conditions,

such as *Hemophilus influenzae* and *Clostridium welchii*, are not routinely tested because special attention to the details of technique is necessary with such organisms. The sensitivity tests described have advantages in that (*a*) they are sufficiently accurate to be clinically useful, (*b*) they can be applied readily to most of the pathogenic bacteria isolated, and (*c*) the results can be read within 48 hours after the initial isolation.

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About the Army Medical Department

The New Army and Air Force Interns

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FROM 1,014 applications, 199 interns were selected for Army internships and 53 for Air Force internships. Both Army and Air Force interns receive their training in Army general hospitals. Of the 252 selectees, 236 have had previous service in the Armed Forces; 44 of the 53 selected by the Air Force had prior service with the Army Air Force; and 28 of the 252 had wartime service in the Medical Service Corps. The General Staff Corps, Infantry, Field Artillery, Coast Artillery Corps, Corps of Engineers, Armored Cavalry, Quartermaster Corps, Military Intelligence Service, Adjutant General's Department, and Ordnance Department are all represented in the former service of our interns. The composite nature of the group is further indicated by the fact that 5 were Marines and 18 were in the Navy during the war.

Five of our interns had advanced to the grade of lieutenant colonel during their former service, 25 to major, and 51 to captain. They all now come in as first lieutenants in the Medical Corps and will not be eligible for promotion until they have finished their internships. While promotions after an internship depend to a large extent on the vacancies which will exist at that time, it is expected that it will be possible to promote Medical Corps officers to the grade of captain sometime during the year following the completion of their internships.

Fifty-four of our interns this year will be assigned to Walter Reed General Hospital, Washington, D. C.; 35 to Letterman General Hospital, San Francisco, Calif.; 34 to Fitzsimons General Hospital, Denver, Colo.; 30 to Madigan General Hospital, Tacoma, Wash.; 14 to William Beaumont General Hospital, El Paso, Tex.; 24 to Tripler General Hospital, Honolulu, T. H.; 11 to Gorgas Hospital, Ancon, C. Z.; and 50 to Brooke General Hospital, San Antonio, Tex. Many of the selectees had appointments in other Army hospitals that have since been closed and have had changes in their assignments. These reassignments were accomplished without difficulty and without detri-

[1] Personnel Division, Office of the Surgeon General, Department of the Army.

ment to the internship programs in any of the remaining hospitals. All training spaces are fully authenticated by the Council on Education and Hospitals of the American Medical Association.

In order that interns will get even broader experience, a system of rotation through suitable local Army or Air Force medical installations has been instituted at two of our hospitals. Under this system, many of this year's interns will have an opportunity to serve a few months in station hospitals as well as general hospitals. For example, interns at Walter Reed General Hospital will rotate through a total of 11 services: 4 in obstetrics and gynecology, 2 each at Fort Belvoir Station Hospital and Bolling Field Station Hospital; 3 in general surgery, 1 at Fort Belvoir Station Hospital and 2 at Bolling Field Station Hospital; and 4 in internal medicine in the hospital at the Old Soldiers' Home, Washington, D. C. Interns assigned to Letterman General Hospital may rotate through 11 services in medicine, surgery, obstetrics, and electives at Fort Ord Station Hospital and Camp Stoneman Station Hospital. Other hospitals may work out similar plans with nearby installations that have adequate staffs in the specialty in which the intern is rotated. In every case, the training will remain under the supervision of the appropriate professional service of the parent hospital and not more than 25 percent of the interns assigned will be absent from the parent hospital at any one time under the rotating plan. An intern will be rotated but once and at only one of the satellite installations. It is expected that this plan will acquaint the participating intern with an attractive phase of military life and at the same time afford him the opportunity to render medical care of a limited nature more on his own responsibility than might have been possible in a larger hospital.

Interns were appointed under the cooperative plan agreed on by the Association of American Medical Colleges, the American Medical Association, the American Hospital Association, the American Protestant Hospital Association, and the American Catholic Hospital Association. In selecting interns, special consideration was given this year to participants in the Medical Reserve Officers Training Corps Program and to those who indicated that they were definitely interested in a military career.

Within the past few months the Army, Navy, and Air Force Medical Departments have all agreed in the publication by the Secretary of Defense of standard policies applying to interns and residents. One of the policies requires that interns entering the program after 31 December 1950 will do so with the understanding that they will be required to serve 1 year of active duty for each year of formal internship in a military hospital. This does not apply to the group of interns coming on duty between 1 July 1950 and 31 December 1950.

As in previous years, internships in Army hospitals are rotating in character and are of 12 months' duration. In general, duties of interns correspond to those in civilian hospitals and there is ample opportunity for discussions of problems with both military and civilian teachers in the fields of clinical medicine. On satisfactory completion of 8 months of internship, interns become eligible to apply for appointment in the Regular Army. They will not be commissioned until after the internship has been completed. Interns may also extend their Reserve categories for 1, 2, or 3 years—an opportunity embraced by many of last year's interns in order to further their knowledge of military medicine before definitely electing it as a career.

As the year of internship progresses, many will be interested in what the future holds. Some of this group will want information regarding the basic medical course at the Army Medical Department Research and Graduate School and the Medical Field Service School. Others will be interested in residencies in one specialty or another. Information on all these subjects will be made available from time to time and representatives of the Surgeon General's Office will be available to discuss the various problems now and then during the internship year. All of the assignments to schools and residencies, in which interns are interested will be awarded by means of definite policies that will be made known to everyone. The standing the officer achieves in his internship will have no little weight in the final selection because effort is made to keep everything on a fair and just competitive basis.

Those of us who interned in the Army many years ago look back at this period with nostalgia. It is with all sincerity, therefore, that we welcome this group of interns to our military hospitals. We are sure that many of them will also, as years go by, have the same feeling of pride that we have when we mention our internship classes at Walter Reed, Fitzsimons, or any of the other hospitals that have grown to mean so much in the military establishment.

Meet the 1950 interns:

Army interns

Name	Medical school	Hospital of internship
Anlage, Henry J	St. Louis University	Fitzsimons.
Arzola, Asdrubal	Temple University	Walter Reed.
Asay, Lyal D	Yale University	Brooke.
Askins, John R., Jr	University of Oklahoma	Fitzsimons.
Babb, John L	Ohio State University	Brooke.
Barila, Timothy G	George Washington University	Walter Reed.
Barnett, Arthur J	Georgetown University	Brooke.
Baugh, James E	University of Georgia	Madigan.
Beckner, William W., Jr	Medical College of Virginia	Gorgas.
Beddow, Ralph M	University of Oregon	Walter Reed.
Bennett, Reginald V., Jr	Duke University	William Beaumont.
Billings, Harry H	University of Minnesota	Tripler.
Blair, Robert T	University of Cincinnati	Walter Reed.
Blaschke, John A	University of Oklahoma	Letterman.

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Army interns—Continued

Name	Medical school	Hospital of internship
Bolton, Billy F	Baylor University	William Beaumont.
Borski, Anthony A	University of Colorado	Fitzsimons.
Bosman, Robert I	Duke University	Walter Reed.
Boyson, William A	University of Pennsylvania	Do.
Brand, Roscoe C., Jr	Ohio State University	Brooke.
Breakstone, Gerald J	University of Pittsburgh	Letterman.
Bridgeford, Otis W	University of Cincinnati	Fitzsimons.
Brock, Mason E	Tulane University	Tripler.
Brooks, Donald A	Howard University	Madigan.
Brown, Paul W	University of Michigan	Letterman.
Brown, William E	Ohio State University	Madigan.
Brzica, Stephen M	University of Nebraska	Do.
Buchele, Matthew J	Baylor University	Brooke.
Buckmaster, George A	University of Virginia	Madigan.
Buess, John E	University of Kansas	Do.
Byrne, Haynes C	Medical College of Alabama	Tripler.
Callista, Richard L	Jefferson Medical College	Madigan.
Casey, John J	University of Louisville	Gorgas.
Casper, Robert B	do	Fitzsimons.
Chadwick, John B	University of Rochester	Gorgas.
Cheves, Roswell S., Jr	Columbia University	Walter Reed.
Cleek, Thornton R	Medical College of Virginia	Brooke.
Coats, Daniel T	University of Kansas	Letterman.
Colley, Richard L	University of Louisville	Brooke.
Cornely, John F	Temple University	Fitzsimons.
Craig, Gus A	University of Arkansas	Madigan.
Cutshall, Vernon H	University of Nebraska	Fitzsimons.
Daniels, John R	Ohio State University	William Beaumont.
Deal, John D	University of Georgia	Brooke.
Delia, Claude W	Yale University	Do.
DeSimone, John S	Alabama Medical College	William Beaumont.
Donatelle, Edward P	University of Minnesota	Tripler.
Doyle, Patrick J	Tufts College	Brooke.
Earle, Lyon H., Jr	do	Walter Reed.
Eaves, Charles C	Baylor University	William Beaumont.
Eckstein, John W., Jr	State University of Iowa	Letterman.
Edwards, Thomas S	Tulane University	Brooke.
Elder, Lindsey T., Jr	Harvard University	William Beaumont.
Ellis, Kent	Yale University	Walter Reed.
Engel, Harold L	University of Southern California	Letterman.
Esau, John	University of Pittsburgh	Walter Reed.
Ettinger, Charles	New York University	Do.
Ewart, James A	University of Pennsylvania	Brooke.
Feldmann, Robert J	Harvard University	Tripler.
Ferguson, Robert P	State University of Iowa	Fitzsimons.
Fineman, Milton	University of Pennsylvania	Gorgas.
Finn, Murray E	St. Louis University	Brooke.
Flaxer, Carl	University of Colorado	Fitzsimons.
Fortson, Luther G., Jr	Emory University	Brooke.
Frankhouser, C. MA., Jr	Long Island College	Do.
Frederickson, Evan L	University of Wisconsin	Walter Reed.
Freeman, Ray W	Southwestern University	Brooke.
Fromang, Vernon L	Emory University	Walter Reed.
Geiger, Hugh S., Jr	do	Fitzsimons.
Glenn, James C	University of Oklahoma	Letterman.
Goates, Ralph G	University of Utah	Walter Reed.
Graf, John E	University of Buffalo	Do.
Grant, Arthur E	Western Reserve University	Fitzsimons.
Grant, Norman L	Columbia University	Madigan.
Green, Robert W	University of Pittsburgh	Walter Reed.
Greene, John P	Duke University	William Beaumont.
Grow, Kenneth A	University of Indiana	Letterman.
Gulbrandsen, Oskar S	Johns Hopkins University	Walter Reed.
Hall, Billy V	University of Arkansas	Do.
Hall, Thomas M	Vanderbilt University	Letterman.
Hambright, Rufus R	Duke University	Brooke.
Hamilton, Edward L	do	William Beaumont.
Haney, Joe S	Jefferson Medical College	Brooke.
Hanson, Victor R	University of Oregon	Fitzsimons.
Harris, John E	do	Walter Reed.
Harrison, William V	New York University	Do.
Hawkins, James C	Washington University	Madigan.
Hayes, Maurice L	University of Tennessee	William Beaumont.
Henderson, James E	Western Reserve University	Fitzsimons.
Hesen, John W., Jr	Medical College of Virginia	Walter Reed.
Hillman, Frederick J	Washington University	Madigan.
Hoge, Joseph H	Medical College of Virginia	Fitzsimons.
Hopeman, Alan R	University of Minnesota	Letterman.
Hughes, Francis E., Jr	George Washington University	Walter Reed.
Johnson, Edward M	St. Louis University	Tripler.
Kearse, William O	Emory University	Brooke.
Kellenberger, Robert E	St. Louis University	Do.
Kitchen, Lloyd	Emory University	Tripler.

Army interns—Continued

Name	Medical school	Hospital of internship
Kokernot, Robert H	Baylor University	Brooke.
Kruse, Francis, Jr	University of Colorado	Letterman.
LaTourrette, Verne G., Jr	New York Medical College	Fitzsimons.
Langsjoen, Per H	University of Minnesota	Letterman.
Lawrence, John C	Vanderbilt University	Gorgas.
Levi, George A	Medical College of South Carolina	Tripler.
Lewis, Charles P., Jr	Duke University	Brooke.
Lindner, Janus C	Yale University	Walter Reed.
Littman, Maxwell L	Tulane University	Do.
MacLean, Donald B	Wayne University	Letterman.
Macomber, Peter B	Harvard University	Madigan.
Meeks, Edwin A	Vanderbilt University	Walter Reed.
Metzger, Joseph F	George Washington University	Do.
Miller, Gordon B	University of Southern California	Letterman.
Mizell, Walter S	University of Arkansas	Madigan.
Moore, Carlyle C	State University of Iowa	Letterman.
Morgan, Francis W	University of Nebraska	Madigan.
Morris, John De L. S	Cornell University	Walter Reed.
Mott, Richard H., Jr	George Washington University	Do.
Mounts, Billy W	Georgetown University	Fitzsimons.
Mueller, Harold W	University of Nebraska	Letterman.
Munns, Richard E	University of Kansas	Madigan.
Muth, Jack R	Syracuse University	Letterman.
McCandless, Dean	Duke University	Fitzsimons.
McClanahan, Frank C	University of Nebraska	Gorgas.
McClatchy, Sam P	Bowman Gray University	Tripler.
McCleery, Walters, Jr	Western Reserve University	Do.
McConnell, Bright	University of Georgia	Madigan.
McElroy, George R., Jr	University of Tennessee	William Beaumont.
McGee, Robert R	University of Nebraska	Gorgas.
McGrade, Hugh P	New York Medical College	Letterman.
McLeod, Donald G., Jr	University of California	Tripler.
Nahil, Fred J	Tufts College	Fitzsimons.
Naz, John F	Wayne University	Tripler.
Nelson, Robert C	Western Reserve University	Letterman.
Neyer, John H	do	Brooke.
Nichols, William H., Jr	University of Georgia	Do.
Nicotri, Benjamin	New York Medical College	Walter Reed.
Nora, James C	Wayne University	Madigan.
Norrell, Milton G., Jr	College of Medical Evangelists	Letterman.
O'Sullivan, Donal D	Loyola University	Madigan.
Obourn, Robert L	Washington University	Fitzsimons.
Parrish, Matthew D	George Washington University	Letterman.
Pear, Bertram L	do	Fitzsimons.
Pope, James K	Bowman Gray University	Letterman.
Preston, Charles L	University of Cincinnati	Walter Reed.
Quinn, Robert E	Yale University	Do.
Rankin, Richard E	University of Virginia	Tripler.
Reedy, Jack D	Baylor University	Do.
Reeve, Arnold M	Wayne University	Brooke.
Reister, Philip D	Washington University	Walter Reed.
Richards, Charles E	University of Utah	Do.
Richardson, William L	Duke University	Brooke.
Rippy, William D	do	Walter Reed.
Robinette, Joseph S	University of Arkansas	Brooke.
Rose, John C	Georgetown University	Walter Reed.
Sand, Richard E	Ohio State University	Fitzsimons.
Sanderson, George M., Jr	University of Buffalo	Do.
Scott, Legh R., Jr	Emory University	Walter Reed.
Sellers, Thomas D	Duke University	Letterman.
Shannon, Karr, Jr	University of Arkansas	Madigan.
Shapiro, Norman D	University of Tennessee	William Beaumont.
Sheehy, James L	Stanford University	Letterman.
Sheffler, Paul W	University of Illinois	Brooke.
Sibley, William R., Jr	Baylor University	Do.
Silverman, Leo H	University of Texas	Do.
Simmons, John R	Boston University	Walter Reed.
Simonis, William G	Ohio State University	Brooke.
Slutzky, Gilbert	Wayne University	Gorgas.
Smith, Martin E	Yale University	Walter Reed.
Smith, Noel G	Albany Medical College	Fitzsimons.
Smith, Vastal B	University of Arkansas	William Beaumont.
Smith, W. T	University of Georgia	Brooke.
Spiro, Franklyn C	Syracuse University	Do.
Stalker, Daniel E	Emory University	Do.
Stark, John W	University of Washington	Letterman.
Stephens, William A	Tulane University	Tripler.
Stewart, Robert M	Duke University	Fitzsimons.
Stilgenbauer, Charles	University of Cincinnati	Do.
Stoddard, Darrell C	Jefferson Medical College	Walter Reed.
Stone, Richardson L	University of Georgia	Brooke.
Sulak, Michael	Tulane University	Do.

Army interns—Continued

Name	Medical school	Hospital of internship
Switzer, Walter E	George Washington University	Walter Reed.
Syner, James C	Boston University	Do.
Talley, Thomas P	Emory University	Fitzsimons.
Teller, George W	University of Colorado	Madigan.
Tomson, Nathaniel C	Vanderbilt University	Brooke.
Torrance, Jonathan B	University of Washington	Madigan.
Upton, Albert L	University of Maryland	Letterman.
Van Osdel, Lewis A	University of Colorado	Fitzsimons.
Vineyard, William R	Washington University	Letterman.
Vultee, Frederick E	Yale University	Walter Reed.
Wagner, Loyd R	University of Nebraska	Madigan.
Watson, William R., Jr	University of Pennsylvania	Letterman.
Wells, John H	Meharry Medical College	Madigan.
Wemple, Jay N	Medical College of Virginia	Walter Reed.
Wetzel, Howard R	University of Indiana	Madigan.
Whayne, Harry U	Tulane University	Walter Reed.
Wright, Lloyd T	University of Illinois	Brooke.
Youngs, Harry H., Jr	Duke University	Do.
Zann, Gregory J	New York Medical College	Walter Reed.
Zelechosky, Henry T	Long Island Medical College	Tripler.

Air Force Interns

Adams, Robert H	University of Kansas	Madigan.
Angel, Ronald W	University of Washington	Walter Reed.
Austin, George N	University of Oklahoma	Do.
Bankston, Ingrum W	Alabama Medical College	Letterman.
Beazley, Homer L	Baylor University	Brooke.
Benkelma, Ward E	University of Kansas	Tripler.
Bennett, James E	University of Michigan	Fitzsimons.
Brown, Harry F	University of Southern California	Tripler.
Conn, Fletcher F	University of Nebraska	Letterman.
Crabtree, Sam F	Alabama Medical College	Tripler.
Crantz, Paul E	University of Nebraska	Letterman.
Crews, Louis M	Jefferson Medical College	Madigan.
Demlow, Jack H	University of Indiana	Tripler.
Dewey, Walter W	Baylor University	Letterman.
Does, Charles W	University of Colorado	Do.
Donnell, Alonzo M., Jr	do	Madigan.
Dormon, George	Alabama Medical College	Brooke.
Falke, Clarence G	Southwestern Medical College	Do.
Fraysee, Louis A., III	Duke University	Fitzsimons.
George, John W	University of Indiana	Letterman.
Gilliotte, Benjamin W	Baylor University	Brooke.
Gray, Billy	University of Oklahoma	Do.
Gregory, R. D., Jr	University of Louisville	Madigan.
Hall, Oscar	University of Texas	Brooke.
Hardy, Douglas M	do	Gorgas.
Hensen, James P	University of Georgia	Brooke.
Hundley, John C	Louisiana State University	Do.
Janes, Julian T., Jr	do	Fitzsimons.
Johnson, Chester W., Jr	University of Minnesota	Gorgas.
Jones, Frederick B	Tulane University	Do.
Kilmark, Robert M	University of Georgia	Brooke.
Levine, Robert	Ohio State University.	Walter Reed.
Mann, Edward C	Tulane University	Do.
Marsh, James W	University of Arkansas	Madigan.
Moore, James C	University of Texas	Brooke.
Morgan, Philander D., Jr	Alabama Medical College	Tripler.
McKay, William M., Jr	University of Utah	Madigan.
McKiski, Wendell E	Baylor University	Tripler.
Nicholas, Thomas A., Jr	University of Colorado	Fitzsimons.
Norton, Austin T	St. Louis University	Brooke.
Puckett, Hollis E	University of Louisville	Walter Reed.
Reynolds, George E	University of Michigan	Letterman.
Rock, Herbert G	Harvard University	William Beaumont.
Schwarting, Bland H	Baylor University	Tripler.
Shafer, James A	Jefferson Medical College	Walter Reed.
Simmons, Frederick R	University of Maryland	Do.
Smith, Arthur G	Syracuse University	Do.
Sorensen, Neil F	University of Southern California	Tripler.
Staples, Pelham P., Jr	University of Georgia	William Beaumont.
Tanner, David E	do	Fitzsimons.
Taylor, George E., Jr	University of Buffalo	Walter Reed.
Touchy, Armant C	Louisiana State University	Fitzsimons.
Waddell, William F	Temple University	Do.

The Station Hospital as a Diagnostic and Treatment Center

WARNER F. BOWERS, *Colonel, MC, U. S. A.*[1]

AN INEVITABLE train of events that will greatly increase the importance of the smaller Army hospitals, make assignment there highly desirable, and increase the prestige of medical care at the post level will take place shortly. This end result is one toward which we have been striving and is the goal toward which all of our specialist training has been directed. Soon we can anticipate a well-qualified, highly trained staff in almost all of the clinical specialties at each Army hospital. Before World War II, assignment at such posts as Fort Benning, Fort Riley, Fort Leavenworth, Fort Sill, and many others was considered highly desirable with all of the advantages of quarters and post life. During the war, however, we got into the habit of speaking in terms of thousands of beds and with the wartime evacuation policy, based on shortages of skilled doctors in specialized fields, station hospitals became glorified dispensaries. The connotation thus became fixed that station hospital assignments were for untrained men who could only transfer patients to a general hospital. Unfortunately this was necessary in the early days of the residency training program, but we are about to see a change for the better with the emergence of a fairly large group of trained men available for assignment. No longer will it be necessary to look condescendingly on such an assignment or to threaten resignation at the prospect. In fact, it is predicted that within the next year the emphasis will shift to the point where general hospital assignments will be less sought after than assignment to station hospitals.

Several factors bear on this point. Since there are to be fewer general hospitals, there will be fewer career possibilities in the general hospital system and more trained men will be needed in the station hospitals. As more trained men are assigned to smaller hospitals, a changed evacuation policy will allow any type of treatment to be given

[1] Office of the Surgeon General, Department of the Army.

there, of which the assigned staff is capable. As more work is done in the smaller hospitals fewer patients will require transfer to a general hospital. A smaller number of transfers of major cases will support fewer residency spaces and the residency training will decrease to a level commensurate with our requirements. All of these factors will diminish the distinction between general and station hospitals and lessen the supposed odium connected with a station hospital assignment. This is progress in the right direction but requires a certain change in emphasis in our present thinking. In civilian practice a 200-bed hospital is relatively large and many doctors spend their entire careers working in even smaller hospitals.

In recent years, the value of group clinics has become increasingly apparent as one answer to the unfortunate features of too much specialization. In group practice, experts in various fields can associate themselves for the practice of a high type of medicine and surgery. Why can we not look on our station hospitals as diagnostic and treatment centers, staffed by experts in various clinical fields, practicing a high type of medicine and surgery, with increasing prestige at the post level? Our peacetime mission, in addition to maintaining readiness for war, is to offer medical care to military personnel and their dependents and what could be more appropriate than to render this care in the patients' home atmosphere rather than in a hospital hundreds of miles away? Our own timidity and lack of confidence in ourselves is distressing. The concept of placing a group of well-trained men in each smaller hospital and then letting them go ahead and practice the specialty for which they have been trained should be an inspiration to the physicians and a welcome innovation to their patients.

BOOKS REVIEWS AND BOOKS RECEIVED

Publishers submitting books for review are requested to address them as follows:

The Editor,
United States Armed Forces Medical Journal,
Bureau of Medicine and Surgery, Navy Department,
Washington 25, D. C.

(For review)

The Physiological Basis of Medical Practice, A Text in Applied Physiology, by Charles Herbert Best, C. B. E., M. A., M. D., D. Sc. (Lond.), F. R. S., F. R. C. P. (Canada), *Professor and Head of Department of Physiology, Director of the Banting-Best Department of Medical Research, University of Toronto,* and Norman Burke Taylor, V. D., M. D., F. R. S. (Canada), F. R. C. S. (Edin.), F. R. C. P. (Canada), M. R. C. S. (Eng.), L. R. C. P. (Lon.), *Professor of the History of Medicine and Medical Literature, University of Western Ontario, London, Canada; formerly Professor of Physiology, University of Toronto.* 5th edition. 1,380 pages, illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1950. Price $11.

This well-known and widely acclaimed text has been brought up to date by the inclusion of many important advances in the fields of medical science; some of the older material has been deleted. This book should be in the library of every physician regardless of his specialty, for the practice of medicine is founded upon a thorough knowledge of physiology.—*Capt. J. L. Schwartz (MC) U. S. N.*

Clinical Pathology, Application and Interpretation, by Benjamin B. Wells, M. D., Ph. D., *Professor of Medicine, University of Arkansas, School of Medicine, Little Rock, Ark.* 397 pages; 32 figures. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $6.

The aim of this book is to point out that of the vast array of laboratory tests only a limited number are of practical clinical application and that of these the physician must know when to call for assistance from the laboratory, how to interpret the results and what are the technical and physiologic limitations that must be taken into consideration when interpreting the tests.

It appears to be the author's aim to emphasize that recognition of many diseases is a clinical problem toward which a laboratory test should be confirmatory and not diagnostic, and as he points out that "insufficient or improper use of the laboratory is often evidence of ignorance; excessive reliance on laboratory results is proof of inexperience."

The material is presented according to the functional systems, and for each clinical condition the applicable laboratory procedures are selected and the results are interpreted from a clinical standpoint. The subjects are listed in a manner similar to that in a textbook of medicine and cover infectious diseases, including the diarrheal, venereal diseases, and the mycoses; diseases of the gastrointestinal tract; respiratory system; kidney and urinary tract; diseases of the blood; cardiovascular system; metabolic and endocrine disorders; clinical laboratory studies in surgery; clinical laboratory studies in obstetrics; and the appendix which discusses laboratory aids in diagnosis and lists the normal

values in blood chemistry, normal blood values, cerebrospinal fluid; and the laboratory tests used in the study of jaundice and liver diseases.

This is an excellent book not only for the internist, surgeon, and general practitioner, but also for the laboratory worker.—*Capt. J. L. Schwartz (MC) U. S. N.*

MITCHELL-NELSON TEXTBOOK OF PEDIATRICS, edited by Waldo E. Nelson, M. D., *Professor of Pediatrics, Temple University School of Medicine; Medical Director of Saint Christopher's Hospital for Children;* with the collaboration of 63 contributors. 5th edition. 1,658 pages; 426 illustrations. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $12.

This new edition of a standard text on pediatrics tackles the admittedly difficult problem of encompasing the various aspects of child care in a single volume with admirable thoroughness. Those who are familiar with the fourth edition will find ample evidence of rewriting throughout, with several new names in the list of contributors. The volume contains 306 more pages than the previous edition with new or completely rewritten sections on growth and development; parenteral fluid therapy; drug therapy; anesthesia; congenital malformations; inborn errors of metabolism; the newborn; infection, immunity and allergy; viral diagnosis; streptococcal infections; histoplasmosis; tumors of the neck; congenital heart disease; the blood; mental deficiency; the endocrine system; bones and joints; muscles; burns; and adolescence. The editor is one of the chief contributors and he has done a monumental job of incorporating the advances of the 5 years between editions in the new volume. The two-column page has been retained for the sake of compactness and ease of reading. Extensive references are given at the end of each section. Several useful appendixes appear in the back. An elaborate index which is almost twice the size of that found in the fourth edition is provided.—*Col. W. G. Brandstadt, MC, U. S. A.*

BRIDGES' FOOD AND BEVERAGE ANALYSES, by Marjorie R. Mattice, A. B., Sc. M., *Assistant Professor of Biochemistry, Graduate School of Medicine, College of Medical Evangelists, Los Angeles, Calif.; formerly Assistant Professor of Pathological Chemistry, Department of Medicine, New York Post-Graduate Medical School, Columbia University; Chief Chemist, New York Post-Graduate Hospital; Consultant Chemist, Department of Correction Hospitals, City of New York.* 3d edition, thoroughly revised. 412 pages. Lea & Febiger, Philadelphia, Pa., publisher, 1950. Price $5.50.

This third edition of a classical reference is a complete revision of the second which was published in 1935. It more than achieves its objective of providing analytical data on the largest possible number of food factors.

Newer knowledge in the field of human nutrition and the latest in analytical data have been incorporated. Some old material was deleted and considerable rearrangement of the remaining material was undertaken so as to emphasize the changing points of view. This has necessitated a completely different approach from that of classical biochemistry. The inter-relationships and inter-dependency of the more than 40 specific individual factors now recognized as a part of the picture of normal nutrition are carefully delineated throughout the book. Emphasis is laid on variables which affect the nutritive content of foods and the precise requirements of the individual.

The chapter on vitamins has undergone considerable revision and enlargement and covers the subject as thoroughly as the comprehensive nature of this volume permits. Considerable attention has been given to the effect of various kinds of processing upon nutritive values.

There is data on the sodium and potassium content of approximately 500 representative foods and 150 municipal water supplies. Additional tables which have been incorporated include goitrogenic foods, strained and chopped or junior foods, and Dr. Helen B. Pryor's width-weight tables used in establishing a proper concept of expected weight (up to 24 years of age).

There is a 20-page biobliography arranged topically, which should prove very valuable to those in search of more detailed studies of the subjects thus documented.

This book is highly recommended for use as a reference by clinicians, dietitians, nurses, public health and welfare workers, medical students and consultants in diet preparation.—*Maj. M. E. Perry, U. S. A. F. (WMSC).*

RACES, A Study of the Problems of Race Formation in Man, by Carleton S. Coon, Ph. D., *Curator of Ethnology, University of Pennsylvania Museum, Philadelphia, Pa.*; Stanley M. Garn, Ph. D., *Research Fellow in Anthropology, Forsyth Dental Infirmary for Children, Boston, Mass.*, and Joseph B. Birdsell, Ph. D., *Assistant Professor of Anthropology, University of California, Los Angeles, Calif.* Publication No. 77 American Lecture Series. 153 pages; illustrated. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $3.

This is a very interesting and thought-provoking dissertation in physical anthropology. The authors bring into play many facts and theories relating to the development of the races of man. They highlight the role of natural selection in the production of genotypes and phenotypes and point out the many reasons for their belief that races are developed because of the natural selection which follows mutations. Ninety percent of the 40,000 genes in the human chromosomes control the capacity of the organism for action and reaction to environment, and determine phenotypes, genotypes, and physiologic resistance to disease. Mutations occur because of outbreeding and because of geographic and climatic environment, and technico-cultural advances in a race. In the last chapter they attempt to classify races by types and stock, and present what appears to be a very adequate grouping and classification as well as a physical description of many races.

The physician and dentist, particularly, will find this a very interesting presentation.—*Capt. J. L. Schwartz (MC) U. S. N.*

BOOKS RECEIVED

Receipt of the following books is acknowledged. As far as practicable, they will be reviewed at a later date.

PRINCIPLES AND PRACTICE OF PLASTIC SURGERY, by Arthur Joseph Barsky, M. D., D. D. S., *Attending Plastic Surgeon, Beth Israel Hospital, New York City; Attending Plastic Surgeon, Morrisania City Hospital, New York City; Attending Plastic Surgeon, Bronx Hospital, New York; Attending Plastic Surgeon, Beth El Hospital, Brooklyn, N. Y.; Attending Plastic Surgeon, New York State Rehabilitation Hospital, West Haverstraw, N. Y.; Clinical Professor of Surgery and Associate Surgeon, New York Polyclinic Medical School and Hospital; American Board of Plastic Surgery; American Society of Plastic and Reconstructive Surgery; American Association of Military Surgeons; Associate Member of British Association of Plastic Surgeons; Associate Member of Mexican Association of Plastic Surgery; formerly Lieutenant Colonel, MC., A. U. S.* 499 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1950. Price $10.

ESSENTIAL UROLOGY, by Fletcher H. Colby, M. D., *Chief of the Urological Service, Massachusetts General Hospital; Assistant Clinical Professor of Genito-Urinary Surgery, Harvard Medical School, Boston, Mass.; Urological Consultant, Lakeville State Sanitorium, Middleboro, Mass.* 580 pages; illustrated. The Williams & Wilkins Co., Baltimore, Md., publishers, 1950. Price $8.

1949 YEARBOOK OF OBSTETRICS AND GYNECOLOGY (October 1948–August 1949), edited by J. P. Greenhill, B. S., M. D., F. A. C. S., *Professor of Gynecology, Cook County Graduate School of Medicine; Attending Gynecologist, Cook County Hospital; Attending Obstetrician and Gynecologist, Michael Reese Hospital; Associate Staff, Chicago Lying-In Hospital; Author of Office Gynecology and Obstetrics in General Practice; Co-author of the DeLee-Greenhill Principles and Practice of Obstetrics.* 629 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., publishers, 1950. Price $4.50.

THE PSYCHOLOGIST IN INDUSTRY, by M. E. Stefner, *Research Psychologist, Personnel Division, General Electric Company, Bridgeport, Conn.* Publication Number 79, American Lecture Series. 107 pages; illustrated. Charles C Thomas, Springfield, Ill., publishers, 1950. Price $2.

ADMINISTRATION OF SCHOOLS OF NURSING, by Dorothy Rogers Williams, M. A., R. N., *Lecturer, Administration of Schools of Nursing and Nursing Services, Frances Payne Bolton School of Nursing, Western Reserve University; Executive Secretary, Association of Collegiate Schools of Nursing;* edited by Isabel M. Stewart, M. A., R. N., *Professor Emeritus of Nursing Education, Teachers College, Columbia University.* 288 pages. The Macmillan Company, New York, N. Y., publishers, 1950. Price $4.

PRIMER OF ALLERGY, a guidebook for those who must find their way through the mazes of this strange and tantalizing state, by Warren T. Vaughan, M. S., M. D., *Richmond, Va.* 3d edition, revised by J. Harvey Black, M. D., *Dallas, Tex.* 175 pages; illustrated. The C. V. Mosby Co., St. Louis, Mo., publishers, 1950. Price $3.50.

DISEASES OF THE FOOT, by Emil D. W. Hauser, M. S., M. D., *Associate Professor of Bone and Joint Surgery, Northwestern University Medical School; Attending Orthopedic Surgeon, Passavant Memorial Hospital, Chicago.* 2d edition, illustrated. 415 pages; 195 figures. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $7.

THE NOSE, An Experimental Study of Reactions Within the Nose of Human Subjects During Varying Life Experiences, by Thomas H.Holmes, M. D., *Lester N. Hofheimer Research Fellow in Medicine;* Helen Goodell, B. S., *Research Fellow in Medicine;* Stewart Wolf, M. D., *Associate Professor of Medicine,* and Harold G. Wolff, M. D., *Professor of Medicine (Neurology), Cornell University Medical College,* New York, N. Y., with a foreword by Warfield T. Longcope, M. D., *Professor Emeritus of Medicine, The Johns Hopkins Medical School, Baltimore, Md.* 154 pages; illustrated. Charles C. Thomas, Springfield, Ill., publisher, 1950. Price $4.50.

ROOT CANAL THERAPY, by Louis I. Grossman, D. D. S., Dr. med. dent., *Assistant Professor of Oral Medicine, The Thomas W. Evans Museum and Dental Institute School of Dentistry, University of Pennsylvania.* 3d edition, thoroughly revised. 368 pages; 119 illustrations. Lea & Febiger, Philadelphia, Pa., publishers, 1950. Price $6.50.

ENDODONTIA, by Bernhard Gottlieb, M. D. (University of Vienna), D. M. D. Hon. (University of Bon), LL. D. Hon. (Loyola University, Chicago); *Professor of Oral Pathology and Dental Research, Baylor University College of Dentistry, Dallas, Tex.; Honorary Member of the American Association of Endodontists; formerly Professor and Head of Department of Histologic Research, College of Dentistry, University of Vienna;* Seth Lee Barron, D. D. S., *Assistant Professor of Root Canal Therapy, Baylor University College of Dentistry, Dallas, Tex.;* and J. Hobson Crook, D. D. S., *Associate in Dental Research, Baylor University College of Dentistry, Dallas, Tex.* 177 pages; illustrated. The C. V. Mosby Co., St. Louis, Mo., publishers, 1950. Price, $6.

SURGICAL TREATMENT FOR ABNORMALITIES OF THE HEART AND GREAT VESSELS, by Robert E. Gross, M. D., *William E. Ladd Professor of Child Surgery, Harvard University Medical School, Boston, Mass.* The Beaumont Lecture, Wayne County Medical Society, Detroit, Mich. 2d printing. 72 pages, illustrated. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $2.

INTRODUCTION TO NEUROPATHOLOGY, by Samuel Pendleton Hicks, M. D., *Departments of Pathology of the Harvard Medical School and the New England Deaconess Hospital; formerly Consultant in Neuropathology, National Naval Medical Center;* and Shields Warren, M. D., *Departments of Pathology of the Harvard Medical School and the New England Deaconess Hospital; Director of the Division of Biology and Medicine, U. S. Atomic Energy Commission.* 1st edition. 494 pages; illustrated. McGraw-Hill Book Co., Inc., New York, N. Y., publishers, 1950. Price $10.

PROGRESS IN BIOCHEMISTRY, A Report on Biochemical Problems and on Biochemical Research since 1939, by Felix Haurowitz, M. D., D. Sc., *Professor of Chemistry, Indiana University, Bloomington, Ind.* Interscience Publishers, Inc., New York, N. Y., publishers, 1950. Price $7.50.

BRUCELLOSIS (Undulant Fever), Clinical and Subclinical, by Harold J. Harris, M. D., F. A. C. P., with the assistance of Blanche L. Stevenson, R. N. Foreword by Walter M. Simpson, M. S., M. D., F. A. C. P. 2d edition, revised and enlarged. 617 pages; 111 illustrations, 12 in full color. Paul B. Hoeber, Inc., New York, N. Y., publisher, 1950. Price $10.

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A SHORT HISTORY OF PHYSIOLOGY, by Kenneth J. Franklin, D. M., F. R. C. P., *Professor of Physiology at the Medical College of St. Bartholomew's Hospital.* 2d edition. 147 pages; illustrated. Staples Press, New York, N. Y., publishers, 1950. Price $2.

OCCUPATIONAL THERAPY, Principles and Practice, edited by William Rush Dunton, Jr., M. D., *Founder and Former Editor, Occupational Therapy and Rehabilitation,* and Sidney Licht, M. D., *Editor, Occupational Therapy and Rehabilitation.* 321 pages; illustrated. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $6.

TREATMENT IN PSYCHIATRY, by Oskar Diethelm, M. D., *Professor of Psychiatry, Cornell University Medical College; Psychiatrist-in-Chief, The New York Hospital (Payne Whitney Psychiatric Clinic).* 2d edition. 574 pages. Charles C Thomas, Springfield, Ill. publisher, 1950. Price $8.50.

UROLOGICAL SURGERY, by Austin Ingram Dodson, MC., F. A. C. S., *Richmond, Va., Professor of Urology, Medical College of Virginia; Urologist to the Hospital Division, Medical College of Virginia; Urologist to Crippled Children's Hospital; Urologist to St. Elizabeths Hospital; Urologist to St. Luke's Hospital and McGuire Clinic,* with 12 contributors. 2d edition. 855 pages; 645 illustrations. The C. V. Mosby Co., St. Louis, Mo., publishers, 1950. Price $13.50.

TEXTBOOK OF BACTERIOLOGY, by Joseph M. Dougherty, A. B., M. A., Ph. D., *Dean of the School of Science and Professor of Bacteriology, Villanova College; Fellow of the American Association for the Advancement of Science,* and Anthony J. Lamberti, B. S., M. S., *Instructor in Bacteriology and Parasitology, Temple University School of Medicine; formerly Instructor in Bacteriology, Villanova College; Member of the American Public Health Association.* 2d edition. 491 pages; illustrated. C. V. Mosby Co., St. Louis, Mo., publisher, 1950. Price $5.75.

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GYNECOLOGY, The Teachings of John I. Brewer, by John I. Brewer, B. S., M. D., Ph. D., *Professor of Obstetrics and Gynecology, Northwestern University Medical School; Chief of Gynecology and Obstetrics, Passavant Memorial Hospital, Chicago.* 437 pages; illustrated. Thomas Nelson & Sons, New York, N. Y., publishers, 1950. Price $7.50.

THE 1949 YEARBOOK OF ORTHOPEDICS AND TRAUMATIC SURGERY (October 1948–November 1949), edited by Edward L. Compere, M. D., F. A. C. S., *Associate Professor of Surgery, Northwestern University Medical School; Chairman, Departments of Orthopedic Surgery, Wesley Memorial and Children's Memorial Hospitals; Consultant Orthopedic Surgeon, Chicago Memorial Hospital; Consultant in Orthopedics, U. S. Naval Hospital, Great Lakes, Ill.* 464 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., publishers, 1950. Price $5.

MEDICAL MANAGEMENT OF GASTROINTESTINAL DISORDERS, by Garnett Cheney, M. D., *Clinical Professor of Medicine, Stanford University Medical School.* 478 pages; 29 figures. The Year Book Publishers, Chicago, Ill., publishers, 1950. Price $6.75.

TRANSACTIONS OF THE AMERICAN GOITER ASSOCIATION, 1949 Annual Session, May 26, 27, 28, Hotel Loraine, Madison, Wis. 460 pages; illustrated. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $10.50.

A PRIMER OF VENOUS PRESSURE, by George E. Burch, M. D., *Henderson Professor of Medicine, Tulane University School of Medicine; Senior Visiting Physician, Charity Hospital; Consultant in Cardiovascular Diseases, Ochsner Clinic; Visiting Physician, Touro Infirmary, New Orleans.* 174 pages; illustrated. Lea & Febiger, Philadelphia, Pa., publisher, 1950. Price $4.

OFFICE ORTHOPEDICS, by Lewis Cozen, M. D., F. A. C. S., *Attending Orthopedic Staff: The Orthopedic Hospital, Veteran's Hospital, Los Angeles County Hospital, Cedars of Lebanon Hospital, Los Angeles, and Los Angeles Tuberculosis Sanitarium, Monrovia, Calif ; Assistant Professor of Orthopedic Surgery, College of Medical Evangelists, Los Angeles.* 232 pages; 156 illustrations. Lea & Febiger, Philadelphia, Pa., publishers, 1950. Price $5.

THE 1949 YEAR BOOK OF DRUG THERAPY, November 1948–October 1949, edited by Harry Beckman, M. D., *Director, Department of Pharmacology, Marquette University School of Medicine.* 718 pages; 133 figures. The Year Book Publishers, Inc., 200 East Illinois Street, Chicago 11, Ill., publishers, 1950. Price $4,75.

POSTGRADUATE GASTROENTEROLOGY, as Presented in a Course Given Under the Sponsorship of the American College of Physicians in Philadelphia, December MCMXLVIII. Edited by Henry L. Bockus, M. D., *Professor of Gastroenterology, University of Pennsylvania Graduate School of Medicine.* 670 pages; 258 figures. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $10.

A MANUAL OF CARDIOLOGY, by Thomas J. Dry, M. A., M. B., Ch. B., M. S. in Medicine, *Associate Professor of Medicine, University of Minnesota (Mayo Foundation); Consultant in Section on Cardiology, Mayo Clinic.* 2d edition. 355 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $5.

THROMBOSIS IN ARTERIOSCLEROSIS OF THE LOWER EXTREMITIES. Publication No. 41. American Lecture Series, by Edward A. Edwards, M. D., F. A. C. S., *Diplomate of American Board of Surgery, Clinical Associate in Anatomy, Harvard Medical School; Instructor in Surgery, Tufts College Medical School; Consultant in Peripheral Vascular Disease, Joseph H. Pratt Diagnostic Hospital and Hospital of the Massachusetts Soldiers' Home; Chief of Vascular Clinic, Boston Dispensary.* 74 pages; illustrated. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $2.

MEDICAL GYNECOLOGY, by James C. Janney, M. D., F. A. C. S., *Associate Professor of Gynecology, Boston University School of Medicine; Associate Visiting Gynecologist, Massachusetts Memorial Hospitals.* 2d edition. 454 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $6.50.

CLINICAL NUTRITION, edited by Norman Jolliffe, M. D., F. F. Tisdall, M. D., and Paul R. Cannon, M. D., for the Food and Nutrition Board of the National Research Council. 925 pages; illustrated. Paul B. Hoeber, Inc., New York, N. Y., publisher, 1950. Price $12.

BIBLIOGRAPHY OF OCCUPATIONAL MEDICINE. Vol. 1, 1948. Published by International Labor Office, Geneva, Switzerland. Price $1.

NEW DISCOVERIES IN MEDICINE, THEIR EFFECT ON THE PUBLIC HEALTH, by Paul R. Hawley. 134 pages; illustrated. Columbia University Press, New York, N. Y., publishers, 1950. Price $2.50.

QUINIDINE IN DISORDERS OF THE HEART, by Harry Gold, M. D., *Professor of Clinical Pharmacology at Cornell University Medical College; Attending-in-Charge of the Cardiovascular Research Unit at the Beth Israel Hospital; Attending Cardiologist at the Hospital for Joint Diseases; Managing Editor of the Cornell Conferences on Therapy.* 115 pages. Paul B. Hoeber, Inc., New York, N. Y., publisher, 1950. Price $2.

A TEXTBOOK OF DENTAL ANATOMY AND PHYSIOLOGY, by Russell C. Wheeler, D. D. S., F. A. C. D., *Associate Professor of Anatomy at Washington University School of Dentistry, St. Louis.* 2d edition. 422 pages; illustrated. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $6.75.

WATER AND SALT DEPLETION, by H. L. Marriott, C. B. E., M. D., F. R. C. P., *Middlesex Hospital, London, England.* Publication No. 32, American Lecture Series. 80 pages. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $2.

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THE 1949 YEAR BOOK OF UROLOGY, edited by Oswald S. Lowsley, M. D., F. A. C. S., *Director, James Buchanan Brady Foundation New York Hospital; Visiting Urologist, St. Clare's Hospital; Consulting Urologist, Hospital for Ruptured and Crippled, Peekskill Hospital, etc.; Member, International Urological Association, Pan-American Medical Association, Pan-American Medical Confederation, International College of Surgeons; Officer of the National Order of Merit and Honor of Haiti.* 445 pages; 62 figures. The Year Book Publishers, Inc., Chicago, Ill., publishers, 1950. Price $5.

OPERATIVE SURGERY, by various authors. Edited by Alexander Miles, M. D., LL. D., F. R. C. S. (Ed.), *Consulting Surgeon, The Royal Infirmary, Edinburgh*, and Sir James Learmonth, KCVO., C. B. E., Ch. M., F. R. C. S. (Ed.), *Regius Professor of Clinical Surgery and Professor of Surgery, University of Edinburgh.* 3d edition. 559 pages; illustrated. Oxford University Press, New York, N. Y., publishers, 1950. Price $6.50.

HORMONES IN CLINICAL PRACTICE, by H. E. Nieburgs, M. D., *Research Associate, Department of Endocrinology, and Assistant Professor, Department of Oncology, University of Georgia; Lately Research Endocrinologist, Department of Obstetrics and Gynaecology, British Post-Graduate Medical School, and Clinical Assistant, Endocrine Clinic, Westminster Hospital, London.* 386 pages, illustrated. Paul B. Hoeber, Inc., New York, N. Y., publisher, 1950. Price $5.50.

THE 1949 YEAR BOOK OF NEUROLOGY, PSYCHIATRY AND NEUROSURGERY (December 1948–October 1949). NEUROLOGY edited by Roland P. Mackay, M. C., *Professor of Neurology, University of Illinois; Attending Neuropsychiatrist, St. Luke's Hospital, Chicago.* PSYCHIATRY edited by Nolan D. C. Lewis, M. D., *Director, New York State Psychiatric Institute and Hospital; Professor of Psychiatry, Columbia University.* NEUROSURGERY edited by Percival Bailey, M. D., *Distinguished Professor of Neurology and Neurological Surgery, University of Illinois.* 668 pages; illustrated. The Year Book Publishers, Inc., Chicago, Ill., publishers, 1950. Price $5.

EXHIBITIONISM, by N. K. Rickles, B. S., M. D., *Fellow of the American Psychiatric Association, Diplomate of the American Board of Psychiatry and Neurology; Senior Consultant at the Veterans' Administration Center, Los Angeles; Consultant in Psychiatry to the Office of the Surgeon General, Medical Department, United States Army; and Director of the Psychiatric Center of Seattle.* 198 pages. J. B. Lippincott Co., Philadelphia, Pa., publishers, 1950. Price $5.

THE ARMY OF ISRAEL, by Moshe Pearlman. 256 pages; illustrated. Philosophical Library, New York, N. Y., publishers, 1950. Price $5.

PRACTICAL STATISTICS in Health and Medical Work, by Ruth Rice Puffer, Dr. P. H., *Tennessee Department of Public Health*, with foreword by Hugo Muench, M. D. 238 pages; illustrated. McGraw-Hill Book Co., Inc., New York, N. Y., publishers, 1950. Price $3.75.

HARVEY CUSHING, Surgeon, Author, Artist, by Elizabeth H. Thomson. Foreword by John F. Fulton. 347 pages; illustrated. Henry Schuman, Inc., New York, N. Y., publisher, 1950. Price $4.

COAGULATION, THROMBOSIS, AND DICUMAROL, with an Appendix on Related Laboratory Procedures, by Shepard Shapiro, M. D., *Assistant Professor of Clinical Medicine, New York University College of Medicine; Visiting Physician, Third (New York University) Medical Division, Goldwater Memorial Hospital; Associate Physician, Lincoln Hospital;* and Murray Weiner, B. S., M. S., M. D., *Fellow in Medicine, New York University College of Medicine; Research Assistant, Third (New York University) Medical Division, Goldwater Memorial Hospital; Assistant Visiting Physician, Willard Parker Hospital Chest Service; Clinical Assistant Visiting Physician, Bellevue Hospital.* 131 pages. Brooklyn Medical Press, New York, N. Y., publishers, 1950. Price $5.50.

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PRACTICAL NEUROLOGICAL DIAGNOSIS, With Special Reference to the Problems of Neurosurgery, by R. Glen Spurling, M. D., *Clinical Professor of Surgery (Neurosurgery), University of Louisville School of Medicine, Louisville, Ky.* 4th edition. 268 pages; illustrated. Charles C Thomas, Springfield, Ill., publisher, 1950. Price $5.

A MANUAL OF BANDAGING, STRAPPING AND SPLINTING, by Augustus Thorndike, M. D., F. A. C. S., *Associate in Surgery, Harvard Medical School; Chief Surgeon to the Department of Hygiene; Harvard University.* 2d edition. 148 pages; illustrated. Lea & Febiger, Philadelphia, Pa., 1950. Price $2.

KINESIOLOGY, The Mechanical and Anatomic Fundamentals of Human Motion Illustrated, by Katharine F. Wells, Ph. D., *Assistant Professor, Graduate Department of Hygiene and Physical Education, Wellesley College.* 478 pages; 224 figures. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $4.75.

GENITO-URINARY SURGERY, by Sir John Thomson-Walker, D. L., M. B., C. M. Ed., F. R. C. S. Eng., *Consulting Urologist and Emeritus Lecturer on Urology, King's College Hospital; Consulting Surgeon, St. Peter's Hospital; President V Congress of Société Internationale d'Urologie; Hunterian Professor Royal College of Surgeons 1907; Lettsomian Lecturer, 1930; President Medical Society of London, 1933.* Edited and revised by Kenneth Walker, M. A., M. B., B. C. (Cantab.), F. R. C. S. Eng., T. I. C. S., *Jacksonian Prizeman and Hunterian Professor, Royal College of Surgeons, 1911, 1922, 1924, 1933; Emeritus Surgeon to the Genito-Urinary Department, Royal Northern Hospital; Urologist, Hornsby Central and Dartford County Hospitals; Member of La Société Internationale d'Urologie; Fellow of International College of Surgeons.* 3d edition. 956 pages; with 25 color and 33 black-and-white plates, and 282 illustrations in the text. Paul B. Hoeber, Inc., New York, N. Y., publisher, 1950. Price $15.

THE CYTOLOGIC DIAGNOSIS OF CANCER, by the Staff of the Vincent Memorial Laboratory of the Vincent Memorial Hospital; *a Gynecologic Service affiliated with the Massachusetts General Hospital, Boston, Mass.; the Department of Gynecology, Harvard Medical School.* Published under the sponsorship of The American Cancer Society. 229 pages, illustrated. W. B. Saunders Co., Philadelphia, Pa., publishers, 1950. Price $6.50.

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